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Tuesday, April 29, 2025

08:00 – 10:00 Session 1, Panel I

Cerebellar circuit elements for the control of limb movement

Ayesha Thanawalla ¹, Alice Geminiani ², Abdulraheem (Abed) Nashef ³, Meike Van Der Heijden⁴ ¹ Salk Institute for Biological Studies, ² Champalimaud Center for the Unknown, ³ University of Colorado School of Medicine, ⁴ Virginia Tech Discussant: Eiman Azim

The ability to perform a wide repertoire of movements with precision and to maintain accuracy despite environmental changes relies on neural circuitry in the central nervous system. The cerebellum has long been known to play a critical role in controlling movement and adapting to environmental perturbations. The cerebellum is thought to refine and adapt movement through learning and implementing an internal model that predicts the outcome of motor commands, rapidly adjusts ongoing movement, and reduces error on subsequent actions. Crucial to its ability to learn, Purkinje cells in the cerebellar cortex receive instructive signals from climbing fibers that originate in the inferior olive and synapse onto Purkinje cells, whose dendrites are major sites for plasticity in the cerebellum. While the cerebellar cortex is thought to be the computational hub of the cerebellum, the cerebellar nuclei receive input from the Purkinje cells and, through its widespread connectivity, communicate with the brain and spinal cord, allowing the cerebellum to influence downstream motor structures. Defining how specific components orchestrate cerebellar learning and motor refinement at a circuit level benefits from a cell type- and pathway-specific approach. By describing recent advances in our understanding of the role of distinct cerebellar circuit elements, this panel aims to emphasize the insights into cerebellar function obtained through cell type-specific approaches in mice. Four speakers were selected for their ongoing work exploring distinct components of cerebellar circuitry. Alice Geminiani (Carey lab) will present optogenetic evidence that climbing fibers provide instructive signals for locomotor adaptation, thus being essential for cerebellar control of whole-body limb movement. Abed Nashef (Person lab) will describe a Purkinje neuron rate and synchrony code that is correlated with specific kinematic features during skilled reaching movements, shedding light on the interaction between Purkinje neurons and the cerebellar nuclei that facilitate online control of movement. Ayesha Thanawalla (Azim lab) will present work defining distinct cerebellar output networks and the rapid bidirectional control of forelimb kinematics and muscle activity by cerebellar nuclear neurons. Meike van der Heijden will describe the neural activity of cerebellar nuclear neurons that distinctly represent cerebellar-associated motor disorders - tremors, ataxia, and dystonia. Eiman Azim will lead a panel discussion focussing on key themes, including: a) How cell-specific interrogation of neural circuits is revealing new insight into cerebellar function; b) How distinct cerebellar circuit elements may function in motor learning vs motor execution; c) The degree to which disruption in any of these pathways influences cerebellar-linked movement disorders; d) how to facilitate increased interaction between those studying cerebellar function in mice and primates.

10:30 – 11:05 Early Career Award Presentation and Talk

Prior beliefs for predicting movements: from neurons to manifolds

Devika Narain, Erasmus Medical Center

Timing and motor control are inexorably linked, and from this interplay emerge various feats of motor precision that pervade the animal kingdom. Yet, laboratory measurements of the timing of movements are riddled with variability and biases that paint a contrasting picture. Previous work has sought to resolve this conundrum using Bayesian theory, which formalizes how prior beliefs about temporal variables shape precise actions under environmental uncertainty. While these frameworks account for various behaviors in different domains, the neural mechanisms underlying the acquisition and use of such prior beliefs continue to elude us. Here, we propose a role for cerebellar circuits in acquiring prior knowledge to shape rudimentary predictive motor behaviors, such as the conditioned eyelid response in Pavlovian eyeblink conditioning. We will show evidence that cerebellar Purkinje cells encode probability distributions of the stimuli and propose a mechanism for how this manifests in the kinematics of the motor output. Furthermore, at the population level, we will show that cerebellar cortical dynamics assume a topological organization in the form of curved manifolds, which encode prior knowledge along the curvature of these topologies. In the second part of the talk, we will present methodological work that aims to unravel topologies and embed these in their intrinsic dimensions to decode task-relevant information. Towards the end, we will use this method to test the hypothesis that the curvature of neural manifolds encodes prior knowledge in sensorimotor timing tasks. Overall, we will propose a neural mechanism for how prior beliefs for the temporal control of movements are acquired by neurons and eventually encoded in the topologies of populations, while adhering to the predictions of normative theory that explain the emergence of precise sensorimotor timing behaviors.

11:05 – 13:05 Session 2, Individual II

OS1.1 - Neuroethology of bodily and manual actions in freely moving monkeys

Luca Bonini ¹ ¹ University of Parma Presenting Author: Luca Bonini

Decades of brain research on the cortical motor system have leveraged nonhuman primates to investigate the anatomo-functional organization of voluntary, goal-directed actions. However, the concept of "goal" and its relationship to the voluntary nature of an action remain widely debated. Studies using intracortical microstimulation (ICMS) have revealed that the frontal motor system encodes final postures of multiple body parts resembling those seen in natural actions. Single-neuron recordings suggest that premotor neurons encode the achievement of specific outcomes, such as reaching a spatial location or obtaining a piece of food, often independently of the sequence of extension-flexion movements or even the effector used to achieve them. This supports the idea that goal coding is a key organizational principle of the premotor cortex. However, these studies are derived from laboratory experiments in restrained contexts (RCs), under the assumption that this knowledge generalizes to freely moving contexts (FMCs). To date, no study has directly investigated the premotor control of natural actions in freely moving monkeys.

To fill this gap, we developed a neuro-behavioral platform enabling stepwise wireless recording of the same premotor neurons in both RC and FMC while filming two monkeys' behavior with a multicamera system. We found that neurons often encoded the same hand and mouth actions differently in RC and

FMC. Furthermore, in FMC, we identified cells selectively encoding actions untestable during RC and others displaying mixed selectivity for multiple actions, consistent with an organization based on cortical motor synergies rather than action goals at different levels of complexity. Interestingly, cross-context decoding of the actions testable in both contexts demonstrated that neural activity in FMC is richer and more generalizable to RC than vice versa, possibly due to the coordinated control of head movement with specific effectors, such as the hand and the mouth, as revealed by head-free ICMS. During reaching-grasping actions directed at objects of different sizes in FMC, we could accurately decode both head movements and grip types, suggesting the existence of previously overlooked synergistic control of distal and proximal motor components in the premotor cortex underlying the flexible organization of primate natural actions.

Our findings support the relevance of neuroethological approaches in unveiling the neural bases of spontaneous, natural behaviors.

OS1.2 - Motor cortical influence during ethological motor behavior

Andrew Miri¹, David Xing¹, Amy Kristl¹, Natalie Koh¹, Zhengyu Ma¹ ¹ Northwestern University Presenting Author: Andrew Miri

It remains poorly resolved when and how motor cortical output directly influences muscle activity through descending projections. The involvement of motor cortex in motor learning and movement preparation complicates the interpretation of lesion and other inactivation results vis-à-vis movement execution, as disturbance to processes on which execution depends can impede execution itself. Direct motor cortical influence could take several possible forms: motor cortex could drive the totality of limb muscle activity patterns, it could participate in unison with the rest of the motor system in generating motor output without playing a necessary role, or it could selectively influence particular components of muscle activity, such that it informs ("instructs") ongoing muscle activity pattern.

To address when and how motor cortical output directly influences muscle activity, we combined optogenetic silencing, electromyography, and Neuropixels recording in mice performing a naturalistic climbing behavior where they effectively traverse an unpredictable terrain. We found that during climbing, the caudal forelimb area (CFA, rodent homolog of forelimb M1) informs muscle activity pattern, acting mainly by selectively exciting certain muscles while exerting smaller, bidirectional effects on their antagonists. Analysis of Neuropixels recordings identified components of CFA activity that correlate with its short latency influence on muscles. These components partially overlap with those that correlate with muscle activity, but are entirely different from those that correlate with forelimb kinematics. This suggests that selective motor cortical influence does not rely on the activity components the field has traditionally focused upon. We also discovered that a substantial fraction of CFA neurons are primarily active during a very limited subset of the forelimb muscle activity states that occur during climbing. This is analogous to the firing of many hippocampal neurons only at particular locations within an environment. These CFA firing patterns are not consistent with the idea that motor cortical activity is well-described as a low-dimensional linear dynamical system.

We have also extended our approach to mice freely exploring an arena that elicits a broad range of naturalistic behaviors, including stereotyped, species-typical behaviors like eating and grooming, and those that challenge agility and dexterity like climbing and walking on an irregular grid. Results here suggest that selective direct motor cortical influence extends to a broad range of naturalistic behaviors. We have also found that CFA's influence on muscles during climbing is substantially larger than during single-forelimb reaching, suggesting a substantial behavioral dependence of direct motor cortical

influence. Other results indicate that this variation across behaviors extends to CFA's interactions with the rostral forelimb area, the rodent homolog of forelimb premotor cortex, as well.

OS1.3 - Motor cortical dynamics during reaching connect posture-specific attractors

Mehrdad Kashefi ¹, Jonathan Michaels ², Joern Diedrichsen ¹, J. Andrew Pruszynski ¹ ¹ Western University, ² York University Presenting Author: **Mehrdad Kashefi**

One of the central questions in motor neuroscience is how the population of motor cortical neurons control voluntary movement. Much of our current understanding of this question is based on so-called center-out reaching tasks that involve reaching from a single start location to various spatial targets — a situation that confounds reach direction with limb posture at the spatial target. Because of this confound, previous studies lack the required condition variability to probe the geometry of neural dynamics (NDs) for movements across different postures and extents. To address this confound, we trained two macaques to move their arm between all possible combinations of five targets located on the vertices and at the center of a rectangle in a 2D exoskeleton (KINARM). This target geometry allowed us to dissociate the abstract cue of the final target from the direction of the reach in certain trial types. For example, diagonal reaches included movements with the same start location and in the same direction but with different extents. Similarly, some reaches shared the same final target and direction but began from different starting locations. We used Neuropixels probes to record single-unit activity from multiple brain regions in two monkeys. In Monkey M, we recorded from primary motor cortex (M1; N=962) and dorsal premotor cortex (PMd; N=833). In Monkey P, we recorded from M1 (N=1310), PMd (N=620), the supplementary motor area (SMA; N=590), pre-SMA (N=310), dorsolateral prefrontal cortex (dIPFC) (N=380), and the internal segment of the globus pallidus (GPi, N=549). In both monkeys, in M1 and PMd, we observed an elegant compositional arrangement of NDs for movement with different postures, extents, and directions with two striking features. First, a posture subspace with attractor points for each spatial target. These attractors were visited whenever the arm rested in its respective target before or after the reach. Second, rotational dynamics that linked the attractor points. These rotational patterns were aligned such that more similar rotational dynamics were associated with more similar reach directions. In monkey P, we could decode start and end locations and movement extent from all recorded sites, though dynamics' geometry differed significantly across regions. To gain mechanistic insight, we trained recurrent neural networks (RNNs) to control a biomechanical arm in a 2D workspace and analyzed their NDs in the same 5-target task. A posture subspace emerged consistently across training parameters. However, RNN dynamics most closely resembled M1/PMd when two factors were applied: (1) regularization of hidden activity smoothness and (2) a spinal RNN module between the main RNN and the arm model. Our work provides fundamental insight into the geometry of NDs in the primate motor cortex during self-initiated reaching, with important implications for brain-computer interface design.

OS1.4 - Inferring the neural control signals that drive locomotion in larval zebrafish

Thomas Soares Mullen ¹, Marine Schimel ², Adrien Jouary ¹, Katharina Koetter ³, Joanna Yen Na Lau ⁴, Ruben Portugues ³, Guillaume Hennequin ⁵, Isaac Bianco ⁴, Michael Orger ¹ ¹ Champalimaud Foundation, ² Stanford University, ³ Technical University of Munich, ⁴ University College London, ⁵ University of Cambridge Presenting Author: **Thomas Soares Mullen** A key function of the brain is to control movements. In larval zebrafish, movements are controlled by descending input from the brainstem to the spinal cord. How these inputs control different parameters of movement is not completely understood. Prior categorical approaches limit the ability to model continuous control schemes effectively. Here, we take an optimal control theory approach to behavioural modelling and argue that movements can be understood as the output of a controlled dynamical system. Leveraging a rich behavioural dataset, our goal is to identify both the latent control signals and the underlying dynamics that make up the locomotor repertoire of the zebrafish larvae. Learning the dynamics of a system driven by unobserved inputs is a challenging system identification problem. We addressed the latter using the iLQR-VAE method, proposed by Schimel, M., et al. (ICLR, 2022), which combines variational inference with optimal feedback control to learn a latent input-driven dynamical system that captures behaviour output. Our findings demonstrate that this repertoire can be effectively generated through a sparse control signal driving a latent RNN. Moreover, the network's latent space encodes kinematic swim features and preserves structures of previously defined bout categories. Intriguingly, we see that the latent dynamics for generating tail movements are shared with pectoral fin dynamics for certain bout types. Interestingly, zebrafish transparency allows for measurements of brain-wide neural activity. While these typically require the fish to be head-fixed, which limits their locomotor repertoire, we were able here to use the dynamical system trained on freeswimming behaviour, and perform inference on head-restrained movements under the constraint of those dynamics. This allowed us to compare the control space of head-fixed movements with freeswimming behaviour. We conducted preliminary analyses to explore the relationship between the inferred control signals and neuronal activity. Our model-based approach offers a new paradigm for disentangling supraspinal neuronal activity from head-fixed fish based on parameters from naturalistic free-swimming behaviour.

OS1.5 - Population dynamics in the motor control and restoration of head stabilization driven by vestibular pathways during locomotion

Ruihan Wei¹, Oliver Stanley¹, Adam Charles¹, Kathleen Cullen¹ ¹ Johns Hopkins School of Medicine Presenting Author: **Ruihan Wei**

Vestibulospinal reflexes are essential for maintaining balance and head stability during locomotion. Individuals with vestibular sensory loss suffer from severe gaze instability and postural imbalance, significantly impairing their mobility. The vestibulo-collic reflex in particular, which activates neck muscles in response to head movement, is thought to play a central role in stabilizing the head during locomotion. We thus sought to better understand vestibular contributions to head stability and motor control strategies across different locomotion contexts, as well as to determine the effectiveness of prosthetic vestibular stimulation at restoring function. We recorded single and multi-motor unit activity in the splenius capitis and sternocleidomastoid muscles using intramuscular EMG in normal monkeys, monkeys with complete bilateral vestibular loss (BVL), and BVL monkeys during head-coupled vestibular prosthetic stimulation. Head and trunk positions were tracked using a head-mounted 6D motion sensor and marker-based tracking systems, while limb movements were analyzed using high-speed video and DeepLabCut. Single and multi-motor unit activity and head stabilization were evaluated during overground and treadmill walking at various speeds. Principal components analysis was applied to the EMG data to quantify population muscle activation for each locomotor context.

In normal monkeys, neck motor unit recruitment was gait phase-locked and antagonistic, facilitating effective head stabilization under various walking conditions. Principal component analysis revealed a consistent activation geometry that scaled with speed during treadmill walking. In contrast, speed-

matched overground walking displayed a distinct geometry with heightened neck muscle responses and enhanced head stabilization. Following bilateral vestibular loss, monkeys exhibited pronounced head oscillations and inadequate compensation for body motion, with reduced phase-locking of neck muscle activity. BVL monkeys failed to adopt a consistent strategy across speeds, although overground walking retained a unique activation geometry compared to speed-matched treadmill locomotion. With headcoupled vestibular prosthetic stimulation, the head motion became more stable, and the gait phasedependent modulation of neck muscle recruitment was restored. Population-level muscle activity regained a motor control strategy again displaying a consistent activation geometry that scaled with speed during treadmill walking and a unique activation geometry during overground walking.

In summary, our results first reveal the presence of population-based motor strategies within and between conditions during simple, innate behaviors, which enable flexible control of head stabilization. In addition, our findings demonstrate the critical role of the vestibular system in coordinating neck motor activity to generate compensatory head movements, ensuring head stabilization in space during locomotion. Finally, our results indicate that prosthetic stimulation can restore the control strategies that the brain uses to maintain balance and head stability during natural behavior, which may provide a foundation for advancing the treatment of vestibular dysfunction by improving strategies for restoring effective locomotion in affected individuals.

OS1.6 - Hierarchical model balancing efficiency and safety in human motor control

Tjasa Kunavar¹, Jan Babic¹, Erhan Oztop², Mitsuo Kawato³

¹ Jozef Stefan Institute, ² Ozyegin University, ³ ATR Brain Information Communication Research Laboratory Presenting Author: **Tjasa Kunavar**

Our research presents a novel perspective on motor learning, exploring how ecological fitness (organism's specific traits and abilities that aid survival in its environment) factors into human motor control. Our sensorimotor system is crucial for ecological fitness since it enables adaptive movement control vital for survival. We delve into how ecological factors contribute to survival by enhancing movement efficiency, while considering the risk of injury associated with failure. Existing motor control theories, which primarily focus on isolated body movements, often neglect these ecological aspects. By redefining computational motor control optimality to incorporate ecological fitness, we propose a strategy that alternates between success-driven efficiency and failure-driven safety. This insight was made possible by an experimental paradigm specifically designed to challenge the sensorimotor system with the realistic possibility of failure and injury risk, underscoring the robustness of the adaptive strategies we identified. Our experimental paradigm involved whole-body squat-to-stand motions with novel backward force perturbations. An integral part of the learning process were failures - movements when the participant lost postural balance and had to make corrective steps to prevent a fall. Participants adapted to the perturbed squat-to-stand movements and dramatically reduced failures, while showing various adaptations to prevent falls. We show that computational motor learning mechanisms of the brain are not flat and utilize hierarchical organization for efficiency, adaptability and robustness. Our data suggests a top-level ecological controller in human motor learning, optimizing for safety or efficiency based on failure or success, to form motor plans to be used by lower-level control. Adaptation of motor plan occurs through fast reinforcement learning mechanism after failed execution of motion. To achieve the intended plan, motor control processes encompass internal model learning and feedback gain tuning mechanisms in addition to the feedback control. Adaptation of motor control is slower and predominantly occurs as a result of adaptation of internal model during movement execution irrespective of movement success. This new model provides a more holistic view of human

motor control, integrating risk management in a hierarchical learning system applicable to ecological situations.

15:30 – 17:30 Session 2, Panel II

From motion to action: Neural mechanisms of interceptive sensorimotor control

Tarkeshwar Singh ¹, He Cui ², Neeraj Gandhi ³, Deborah Barany ⁴

¹ Pennsylvania State University, ² Chinese Institute for Brain Research, Beijing, ³ University of Pittsburgh, ⁴ University of Georgia

Discussant: John Douglas Crawford

Interceptive movements, from catching a ball to chasing a toddler running towards the street, represent a complex class of motor behaviors that provide an ideal paradigm for investigating fundamental questions in motor control. Unlike stationary targets, moving targets fundamentally transform sensorimotor demands by requiring precise spatiotemporal coordination, continuous integration, and adaptive error correction. This session brings together four animal and human research programs examining how the brain processes motion signals to guide interceptive movements. The speakers present approaches spanning non-human primate neurophysiology, human TMS, EEG, and behavioral studies to unravel the neural computations underlying interception.

He Cui will present pioneering work in non-human primates performing manual interception of circular moving targets. Their findings reveal that monkeys accurately compensate for both sensory and motor delays during interception. Single-unit recordings demonstrate that posterior parietal cortex encodes planned movement parameters rather than instantaneous visual information, while motor cortex exhibits mixed selectivity for both movement planning and ongoing target motion. Novel analyses of population-level neural dynamics suggest orthogonal encoding of target velocity in motor cortical activity, supporting robust forward predictions for motor planning and timing control.

Raj Gandhi will discuss how the brain overcomes neural processing delays using the saccadic system as a model. Through integrated human behavioral and monkey neurophysiology studies, his work reveals systematic variations in interceptive saccade parameters based on target motion features. Superior colliculus recordings demonstrate that target motion reshapes classical receptive field properties and alters neural response profiles, providing insight into early sensorimotor transformations for interception.

Deborah Barany will present TMS investigations of how visual motion information shapes motor cortical output during interceptive movement preparation. Her studies reveal that corticospinal excitability is selectively enhanced prior to intercepting faster-moving targets, independent of target distance or eye movement strategy. This modulation appears specific to movement preparation rather than motion perception, providing direct evidence for how target motion parameters influence motor system excitability.

Tarkesh Singh will present research on mechanisms of motion processing for postural control and interception. His studies reveal that while young adults utilize both retinal and extraretinal motion signals for posture stabilization, older adults rely predominantly on extraretinal mechanisms. EEG findings demonstrate connectivity between motion-processing areas and premotor regions during motor planning. His work also highlights how extraretinal signals modulate long-latency reflexes to stabilize posture during interactions with moving objects.

Wednesday, April 30, 2025

08:00 – 10:00 Session 5, Panel III

Poking the manifold: leveraging modeling, learning, and perturbations to causally test latent dynamics

Lee Miller ¹, Dan O'Shea ², Alex Cayco Gajic ³, Ian Oldenburg ⁴

¹ Northwestern University, ² Stanford University, ³ École Normale Supérieure, Paris, ⁴ Rutgers University Discussant: Matthew Perich

100 years after Bernstein's pioneering efforts to understand the brain's control of redundant motion, interest has focused on analyses of "neural manifolds", low-dimensional representations of neural activity which result from the redundancy within the brain itself. This approach has led to new insights about motor preparatory activity and the relationship between neural and behavioral dynamics. In addition to the ability to record exponentially larger numbers of neural network models that link task computation to latent dynamics and behavior. These complementary approaches to understanding the relation between neural activity and behavior go well beyond the limitations of correlational analysis of recorded activity.

Miller will begin by providing an overview of the concepts and analytical approaches needed to understand the discipline. He will present data demonstrating the remarkable stability between lowdimensional, latent signals and well-learned behavior. These include data recorded during learning, and in the cage, where the physical constraints of the lab setting are eliminated. The dynamics of the latent signals differ to the extent that linear decoding of EMG fails across the contexts, but the results shed light on how these behaviors are controlled. Next, Cayco Gajic will present modeling studies examining the tension between the need for a stable representation of behavior, while still enabling rapid adaptation with learning. She will describe a multi-region RNN model of the interaction between the motor cortex and cerebellum, capable of learning a visual motor adaptation task, and propose an optogenetic experiment to test its validity. Then, Duncker will describe work combining computational modeling with analyses of neural population responses to optogenetic and ICMS perturbations during reaching. This approach allows her to evaluate hypotheses about the network-level dynamical mechanisms underlying pattern generation in motor cortex. She will show that stimulation in M1 perturbs reaching only to the extent that it alters neural states within an identifiable low-dimensional dynamical subspace. Finally, Oldenburg will describe his pioneering work using holographic optogenetics to control the activity of hundreds of neurons in behaving mice with millisecond precision, allowing him to evoke user-designed population vector activity, and to test predictions in actual neuron networks. Compared to ICMS or typical optogenetic methods, holographic control of network activity promises the ability to manipulate network activity with unprecedented precision.

We seek to engage the audience in a discussion of the strengths and weaknesses of the recording, stimulation, and modeling approaches, and the necessary next steps to advance the field of neuronal manifolds to understand the causal connections linking circuits to activity to behavior.

10:30 – 12:30 Session 6, Individual II

OS2.1 - Motor adaptation in redundant input spaces occurs through changes in both internallygenerated feedforward control and sensory-driven feedback control

Katherine Perks¹, Lydia Smith¹, Sam Burden¹, Amy Orsborn¹ ¹ University of Washington Presenting Author: Katherine Perks

Introduction: To control a familiar motor effector, like a computer mouse, we rely on both sensory information (feedback control) and internal predictions about how the effector works (feedforward control). But how do we adapt to unfamiliar effectors? Human psychophysics studies have identified multiple types of motor adaptation using visuomotor perturbations. However, these experiments often focus on assessing changes in feedforward control and lack methods to simultaneously quantify feedback control. They also use simplified tasks where each dimension of movement is associated with a unique dimension of feedback, which does not reflect the redundancy inherent in natural motor tasks and effectors. Redundancy may create challenges for learning as not all input changes produce distinct feedback. We hypothesize that adapting both feedforward and feedback control is critical to learning redundant sensorimotor transforms. We designed a novel paradigm that combines visuomotor perturbations in a rich input space with a control theory-based task that disentangles the two forms of control (Yamagami 2021; Yang 2021). This allowed us to study feedforward and feedback control changes during input-redundant motor learning in non-human primates for the first time.

Methods: We trained two male rhesus macaques to control the movement of a 1D cursor using unconstrained 3D hand movements. We specified an 'intuitive' initial control axis in 3D space M_i onto which hand position was projected and transformed into cursor position. The monkeys used M_i to perform a 1D tracking task, which consisted of following a pseudo-random moving target while also correcting for a disturbance applied to the cursor. The target and disturbance trajectories contain distinct frequencies, which enables separate quantification of feedforward and feedback control. Once the monkeys were well-trained on the task using M_i , we leveraged the redundant input space to create perturbed control axes M_p , which rotated M_i by 20°, 60°, 90° or 180° (a total of N=8 perturbations, complete in one monkey and in progress in the other). As the monkeys adapted to the perturbations, we recorded their movements and quantified their feedforward and feedback control to link changes in each controller to changes in behavior and performance.

Results: Monkeys adapted to all M_p but adapted faster as they were exposed to more perturbations. This suggests they learned not only the particular M_p but also general learning strategies. Surprisingly, the 180° rotation required the most time to learn, despite sharing the same task-relevant axis as M_i . We found the monkeys used many different strategies to increase the amount of feedback received, including making larger movements early in learning to compensate for less overlap between their movements and M_p . We found performance gains correlated with improvements in feedforward control as well as aspects of feedback control, which has not previously been reported. This supports our hypothesis that motor learning in redundant input spaces involves updating both internally-generated predictions and the way feedback signals are used. Our results provide novel insight into how motor adaptation occurs in previously unstudied contexts and will enable new ways to study the neural mechanisms of motor learning.

OS2.2 - Region-specific neural dynamics and interactions during complex dexterous movements

Ahmet Arac¹, Sanjay Shukla¹, Erica Nagase¹, Alan Yao¹, Nicolas Jeong Lee¹, Kate Santoso¹, Emily Stenzler¹, Kasey Kim¹, David Lipkin¹, Angela Kan¹, Christina Abdishoo¹ ¹ University of California, Los Angeles Presenting Author: Ahmet Arac Complex motor actions, such as reach-and-grasp movements, rely on the coordinated activity of multiple brain regions, each contributing distinct computations to control behavior. To uncover the neural principles underlying this process, we recorded spiking activity across 10 brain regions (primary and secondary motor and primary sensory cortices, multiple regions in caudateputamen, globus pallidus externa and interna, motor nucleus of thalamus, and deep cerebellar nucleus) in mice performing a skilled reach-and-grasp task. Through detailed kinematic analysis, we identified four distinct behavioral phases: a preparatory phase, two movement phases, and a post-grasp phase. Each phase exhibited unique kinematic parameters, highlighting the modular nature of the movement.

Single-neuron analyses revealed that while similar proportions of neurons (60–80%) across regions responded during each phase, the strength of these responses varied. Notably, response strengths were consistently lowest during the first movement phase across all regions, with region-specific variations emerging in subsequent phases, particularly in the primary sensory cortex (S1). Despite these similarities in single-unit activity, dynamical systems modeling revealed distinct, phase-specific computational rules across regions. Using recurrent switching linear dynamical systems (rSLDS) modeling, we demonstrated that neural state transitions aligned closely with behavioral phase transitions in the primary motor cortex (M1) and secondary motor cortex (M2). However, this alignment was less consistent in other regions, underscoring region-specific computational dynamics. The properties of the dynamical rules were also different across phases and regions.

To explore inter-regional interactions, we implemented data-driven recurrent neural network (RNN) modeling combined with in silico perturbation experiments. These analyses highlighted a specialized role for M2 in modulating M1 activity during the pre-grasp phase. This finding was confirmed through optogenetic inhibition of M2 during neural recordings in M1, which disrupted the reach-and-grasp behavior when applied before the grasp but had no effect afterward. Further, RNN-based pairwise inhibition experiments revealed phase-specific influences of other regions on M1, demonstrating a dynamic and context-dependent hierarchy within the motor network.

Additional analyses of trajectory tangling provided insight into neural variability across phases. S1 exhibited significantly higher tangling (as shown before) across trials compared to other regions, while other regions exhibiting low tangling. Intriguingly, M1 tangling remained consistently low across phases, while M2 tangling progressively increased, suggesting a differential role for M2 in shaping motor output.

In summary, our results demonstrate that reach-and-grasp behavior is composed of kinematically distinct phases, each governed by unique neural computations and inter-regional interactions. While single-unit responses often appeared similar across regions, the underlying dynamical rules were highly region- and phase-specific. These findings reveal a sophisticated interplay of hierarchical and parallel processing within the motor network, advancing our understanding of how different brain regions coordinate to execute complex motor tasks.

OS2.3 - Hierarchical state decoding for seamless selection between multiple iBCI functions

Anna Pritchard ¹, Samuel Nason-Tomaszewski ¹, Brandon Jacques ¹, Yahia Ali ², Kaitlyn Tung ³, Payton Bechefsky ⁴, Leigh Hochberg ⁵, Nicholas Au Yong ¹, Chethan Pandarinath ¹

¹ Emory University and Georgia Institute of Technology, ² Georgia Institute of Technology & Emory University, ³ Georgia Institute of Technology, ⁴ Coulter Department of Biomedical Engineering, Emory University and Georgia Tech, ⁵ Brown University

Presenting Author: Anna Pritchard

Intracortical brain-computer interfaces (iBCls) have demonstrated significant potential for restoring control of movement and speech for people with tetraplegia and dysarthria. In previous demonstrations, iBCI users had arrays placed targeting a single control modality (brain areas canonically associated with hand or speech). Recently, BrainGate2 Clinical Trial participant T16 had 4 microelectrode arrays placed in precentral gyrus (PCG) targeting hand (Brodmann's area 6d) and speech (6v&55b) modalities. Recording from multiple brain networks enables multifunctional control, but usability is severely limited without the ability to switch between *functions* (controllable outputs within a modality), as alternatives require either constant activation of all functions or manual switching. Here, we investigate the potential for a hierarchical state decoder to infer the iBCl user's intended functional output. Inspired by at-home iBCI computer use where cursor control may not be a constant intent, we first designed a cursor-and-click task during which T16 was randomly prompted to use various hand or speech functions (e.g. move pinky, speak, think, do nothing). We identified channels that encoded specific functions (e.g. channels modulated differently for think vs say 'bring', or move pinky up vs control cursor with pinky). Trials were classified by condition from all (71% acc. all 9 conds.), hand (75% 4 hand conds.), and speech (67% 5 speech conds.) arrays. This suggests that PCG shows distinctions between not only hand and speech modalities, but also distinct functions within hand and speech. Next, we designed a multifunctional iBCI task where T16 was instructed to sequentially read a sentence, use brain-to-text to type the sentence, and use the cursor iBCI to select incorrect text predictions. Offline, we modeled the data with Hidden Markov Models (HMMs) to distinguish task phases (idle, read, speak, cursor). We compared individual hand- and speech- array HMMs against a single HMM using all arrays for classifying all functions (all/speech/cursor acc. 62%/90%/78% single; 54%/89%/72% dual). Finally, we demonstrated the feasibility of these HMMs to decode T16's functional intent in an online iBCI setting. T16 performed a similar multifunctional task as before, but the cursor and speech decoders were de/activated according to the decoded user intention. Speech (90% acc.) and cursor (70%) classification reflect offline results with minimal latencies for decoded speech onset/offset (-0.83+/-0.73s onset, 0.32+/-0.43s offset). Next we will demonstrate the use of state decoders for switching between functions within a modality (cursor and robot) and integrate function-switching with personal iBCI use. These decoders enable iBCI users to independently switch control between multiple modalities, may enable control of multiple functions within a modality, and can be extended to facilitate multifunctional iBCI control across a multitude of applications.

OS2.4 - A novel peripheral neural interface to manipulate limb movement through myocontrolled optogenetic sensory nerve stimulation

Akito Kosugi ¹, Moeko Kudo ¹, Shiro Egawa ¹, Ken-Ichi Inoue ², Masahiko Takada ², Kazuhiko Seki ¹ ¹ National Center of Neurology and Psychiatry, ² Kyoto University Presenting Author: **Akito Kosugi**

Neural interfaces targeting the peripheral nervous system, such as cochlear implants, are primarily designed to restore lost sensory perception, with relatively few addressing motor functions. While functional electrical stimulation has been used to restore motor functions, it often faces challenges in adapting to dynamic movements due to the difficulty in modulating multiple muscle activities. In this study, we focused on proprioceptive reafferent signals that are generated by one's own movement (reafference). These signals not only contribute to somatosensory perception through transmission to the somatosensory cortex, but also play a crucial role in generating muscle activity via the spinal reflex loop. Since these signals are distributed throughout the spinal cord, their modulation can influence multiple muscle activities through the reflex loop, offering the potential to correct inappropriate dynamic movements. In addition, this event could occur without the need for volitional motor

commands, thereby reducing a cognitive effort to restore motor functions. Here, we propose a novel peripheral neural interface that targets the somatosensory reafferent signal to restore motor functions. Using optogenetics, we specifically modulated peripheral sensory nerve activity during animal's reaching movements to examine the effects of neuromodulation on ongoing movements.

First, we investigated the optimal serotype and administration route of adeno-associated virus (AAV) vectors for selective targeting of large-diameter afferents associated with tactile and proprioceptive sensations in common marmosets. We found that systemic administration through intravenous injection of the capsid variant of a serotype-9 AAV vector (AAV-PHP.B) selectively transduced channelrhodopsin 2 (ChR2) into large-sized dorsal root ganglion (DRG) neurons. In acute electrophysiological experiments, we confirmed the selective activation of large-diameter afferents via optical stimulation to the peripheral nerve.

Next, we trained animals to perform a visually-guided reaching task. After completing the training, we transduced ChR2 into large-sized DRG neurons. During task performance, we applied transdermal optical stimulation to the afferent nerve from the wrist flexor muscles (median and ulnar nerves). When we applied the stimulation by triggering the EMG activity of the agonistic muscle of reaching (triceps brachii muscle), animals exhibited undershot reaching and failed to reach the target. Further analysis revealed that this undershooting was caused by reduced activity in the triceps brachii muscle, which was due to the recruitment of reciprocal inhibitory reflex induced by optogenetic stimulation. These results highlight the significant impact of optogenetic sensory nerve stimulation on ongoing movement. Furthermore, this suggests the potential of a novel peripheral neural interface that targets peripheral sensory nerves to correct overshooting limb movement, such as dysmetria.

OS2.5 - Developing a sensory representation of an extra robotic digit

Lucy Dowdall ¹, Giulia Dominijanni ², María Molina ¹, Edmund Da Silva ¹, Fumiya Lida ¹, Matteo Bianchi ³, Dani Clode ¹, Tamar Makin ¹

¹ University of Cambridge, ² École Polytechnique Fédérale de Lausanne, ³ University of Pisa Presenting Author: Lucy Dowdall

Our motor system relies on somatosensory feedback to inform about the state of our limbs and interactions with our environment. This creates challenges for wearable technology that interface with our sensorimotor system, as they are thought to have 'open-loop' control, with no direct tactile feedback available. However, a neglected area is the natural sensory feedback we can receive from how such devices are worn on, and controlled by, our bodies.

When using an extra robotic finger - the Third Thumb (Dani Clode Design), worn on the side of the hand (the 'palm'), participants can successfully develop a sense of proprioception (Kieliba et al., 2021). This implies the natural sensory feedback can be used to inform about device 'somatosensation'.

To characterise how this natural feedback is experienced, we identified two key components – skin stretch of the palm when the Thumb moves and vibrotactile information when objects engage with the Thumb tip. We then developed two artificial feedback systems for use with the Thumb that replicated these aspects (stretch and vibration) to offer comparison between natural feedback and artificial touch technology. Participants (*N*=20) performed a softness discrimination task (where we expected the skin stretch to excel) and a texture discrimination task (where we expected the vibrotactile to excel) with the natural and artificial systems. People could successfully perform the tasks with the artificial systems, however they performed comparably with the natural feedback, demonstrating we can extract meaningful information from it.

To then explore how our somatosensory system processes this information, we used fMRI to study the representational similarity patterns across the hand and Thumb in primary somatosensory cortex (S1) (*N*=50). We found that after only limited exposure, the brain already organises this tactile input from the Third Thumb in a topographically appropriate manner and in a distinct way from the palm.

Next, we examined how this natural tactile input supports motor learning. Participants completed 7 days of Thumb-hand collaboration training (*n*=30), whilst controls received 7 days of keyboard training (*n*=20). Following this altered finger-synchronisation motor training, we observed reduced inter-finger information content in S1, with larger changes in the Third Thumb group. Importantly, Thumb training produced specific increases in representational similarity between the Third Thumb and biological hand. This integration implies construction of a sensory representation of the Third Thumb in relation to the fingers through their co-usage.

Overall, we have demonstrated the utility of tactile feedback received as a natural by-product of how technologies interface with our body. Our brain can access a sensory representation after only limited exposure to such feedback, which can be integrated with our body following training. Such sensory cues could provide a way of 'closing' the sensorimotor loop.

<u>OS2.6 – Neuro-musculoskeletal modeling reveals muscle-level neural dynamics of adaptive learning in</u> <u>sensorimotor cortex</u>

Mackenzie Weygandt Mathis ¹ ¹EPFL Presenting Author: Mackenzie Mathis

The neural activity of the brain is intimately coupled to the dynamics of the body. In order to predict the sensorimotor consequences of our actions, compelling behavioral studies in humans, non-human primates, and in rodents have shown the existence of internal models — predictive models of our body in the environment. However, the neural computations that update these internal models during motor learning remains largely unknown. There is growing evidence in several sensory areas, such as in the visual and auditory primary cortex, that activity of layer 2/3 encodes sensory prediction errors when unexpected stimuli are presented, which theoretically could serve as a teaching signal. Notably, somatosensory (S1) is essential in rodents and humans learning to adapt arm movements, but, if equivalent prediction errors are observed in S1 has not been established. Lastly, an outstanding question more generally for prediction errors is in which coordinate frameworks would such errors be computed? Here, we directly test whether errors are encoded in S1 during a motor adaptation task in mice. We find that layer 2/3 neurons encode sensorimotor prediction errors (SmPEs), and critically, we identify muscle spaces as the coordinate framework. To do this, we developed a novel 50-muscle model of the adult mouse forelimb that is capable of studying motor control and learning in a physicssimulator. Using model-derived features, we find that during adaptive learning, functionally distinct neurons are mapped onto specific computational motifs. S1 neurons more prominently encode SmPEs, and the neural latent dynamics change in S1 (but not in motor cortex; M1) during this within-session learning. Together, our results provide a new model of how neural dynamics in S1 enables adaptive learning.

15:00 – 17:00 Session 8, Panel IV

The role of Basal Ganglia in complex walking: implications for aging and neurodegenerative diseases

Shuqi Liu¹, Julia Choi², Caterina Rosano¹, Katrina Nguyen³ ¹ University of Pittsburgh, ² University of Florida, ³ University of Colorado Anschutz Medical Campus Discussant: Gelsy Torres-Oviedo

Mobility deficits such as reduced locomotor adaptations and dual-task abilities are common with aging and can represent prodromal signs of neurodegenerative diseases including Parkinson's disease (PD) and Alzheimer's disease and related dementias (ADRD). In fact, mobility decline often precedes cognitive symptoms in ADRD. Therefore, it is reasonable to hypothesize that shared neural mechanisms underlie the diseases that are thought to be motor, such as PD, or cognitive, such as ADRD. Our panel will discuss one such potential neural mechanism: the basal ganglia.

The panel includes experts in human and animal locomotor control, aging, and neurodegenerative diseases. We will show behavioral, electrophysiology, and neuroimaging evidence on the role of basal ganglia underlying complex walking behaviors, the influence of aging, and implications in patients with PD or Mild Cognitive Impairment (MCI), an early stage of ADRD.

Caterina Rosano will discuss results from an epidemiological study showing that striatal dopaminergic neurotransmission, measures through neuroimaging, predicts gait speed changes during dual-tasks in older adults, independent of age, sex, and physiological factors such as muscle strength or joint pain. The mechanisms underlying this relation and its therapeutic implications will be discussed.

Shuqi Liu will present data linking two behaviors critical for mobility, dual-task walking and locomotor adaptation, in young and older adults with or without MCI. She will argue that walking tasks that are typically automatic and controlled by subcortical structures like the basal ganglia will require cortical compensations with aging, but the availability of the compensation is impacted by cognitive health.

Julia Choi will present locomotor adaptation data in PD patients with Freezing of Gait (FoG). Behavioral and electrophysiological data from patients who underwent Deep Brain Stimulation (DBS) in the globus pallidus internus (GPi) show that impaired walking adaptation is related to distinct GPi oscillations in PD with FoG. She will discuss how combining bidirectional DBS with locomotor adaptation can provide insights into the brain activity underlying gait dysfunction in PD.

Katrina Nguyen will show locomotor adaptation results from mice with normal vs. pathological dopaminergic circuits. She will revisit classic locomotor paradigms in freely behaving mice, while leveraging new tools for detailed body pose estimation to assess how movements evolve longitudinally in healthy and unilaterally dopamine depleted mice. She will share data for pathological behaviors that emerge and normal behaviors that recover over the course of learning.

In sum, we will show that basal ganglia dysfunction could underlie neurodegenerative diseases predominantly observed in older populations and have both motor and cognitive symptoms, and discuss the potentials of these non-invasive approaches for early detection and interventions in PD and ADRD.

Thursday, May 1, 2025

08:00 - 10:00 Session 9, Panel V

Sensorimotor control of the tongue during feeding and voluntary movement sequences

Nicholas Hatsopoulos ¹, John Barrett ², Ellen Lumpkin ³, Dan O'Connor ⁴ ¹University of Chicago, ² Northwestern University, ³ University of California, Berkeley, ⁴ Johns Hopkins School of Medicine Discussant: Callum Ross The tongue is an important structure for organismal survival because it mediates the critical functions of feeding and, in some species, communication. The neural control of the tongue in human speech has received much attention; in contrast, the neural control of the tongue and associated orofacial structures during feeding is understudied, especially when compared with control of the limbs and eyes. The tongue is particularly interesting because it is a mid-line, soft body hydrostat that possesses no bones or joints and yet its movement and shape can be exquisitely controlled. What is the role of sensory feedback in guiding tongue movements and posture, and what is the role of cortex in this control and coordination with other organs, such as jaws and hands? Nicho Hatsopoulos will begin by presenting evidence that orofacial areas of primary motor (M1of) and somatosensory (S1of) cortices carry detailed information on tongue kinematics during feeding in macaque monkeys. By recording implanted marker kinematics using a novel 3D x-ray video radiography technology together with single unit activity from electrode arrays implanted in M1of and S1of, he will show how neural population activity from these areas can decode kinematic and shape variables across the feeding sequence with accuracies comparable to those of the arm and hand. Ellen Lumpkin will discuss the role of the sensory periphery in feeding by focusing on mechanosensation of the tongue and palate. Using neuroanatomical and calcium imaging approaches, she has found that the complement of trigeminal mechanosensory neurons innervating the tongue is distinct from those innervating palate and skin. In particular, the majority of lingual mechanosensory neurons respond transiently to dynamic stimuli whereas the palate is densely innervated by slowly adapting, pressure-sensitive afferents that innervate epithelial Merkel cells. John Barrett will expand on the functional role of the tongue by considering how it can be used to reach for and retrieve food pellets by coordinating its movements with the jaw and hand in mice. He will characterize the motor syntax of the tongue consisting of an initial reach, deformation of the tongue tip around the pellet, retraction, and finally securing the pellet by coordinated action of the tongue, jaw and hands. He will present on-going work examining neural activity patterns in orofacial and hand primary motor cortices together with 3D kinematic tracking of the tongue and hand to understand how the cortex mediates this coordinated behavior. Finally, Dan O'Connor will present results on the sensorimotor control of voluntary tongue sequences with mice trained to perform "sequence licking" tasks. He will focus on how ascending sensory signals from tongue mechanoreceptors and jaw muscle spindle afferents are integrated with motor signals from regions of primary somatosensory and motor cortices to guide flexible, goal-directed tongue/jaw movements.

10:30 – 12:30 Session 10, Panel VI

<u>Single-neuron dynamics: unveiling the single-cell type underpinnings of behavior, disease phenotypes,</u> and therapy in motor disorders

Marco Capogrosso ¹, George Mentis ², Kimberly Dougherty ³, Claudia Kathe ⁴, Thomas Hutson ⁵, Serena Donadio ⁶

¹ University of Pittsburgh, ² Columbia University, ³ Drexel University, ⁴ University of Lausanne, ⁵ Wyss Center for Bio and Neuroengineering, ⁶ Rehab and Neural Engineering Discussant: Marco Capogrosso

With the emergence of high-count neurotechnologies and new mathematical tools we've been witnessing the development of population neural dynamics as a central tool to study motor control. This framework seems to overcome the limitations on the analyses that can be conducted at a single neuron level to provide insights on the computations executed by large neural networks during motor planning and execution. However, while we enjoy the explosion of this scientific framework, we shouldn't neglect

that single neuronal types have profound impact on behavior, particularly in specialized circuits. Indeed, neurons are not static input-output functions, but rather complex biochemical structures that adapt in response to changes in the environment. In this panel, we will explore how adaptations of single neuronal types in the spinal cord underpin the emergence of motor phenotypes in major motor disorders. We will show how single-cell type changes drive motor recovery and how they can be targeted to develop therapies. To build our case we present a 5 speakers panel divided in two sessions: a basic science session and a new therapies horizon session. In the basic science session Dr. Mentis will demonstrate how the adaptation of a single ion channel in motoneurons is responsible for widespread muscle weakness and atrophy in Spinal Muscular Atrophy (SMA), a progressive motoneuron disease. Importantly, Dr. Mentis will introduce the idea that these changes are driven by homeostatic adaptation rules that re-shape the function of motoneurons in response to SMA-altered circuits. Following this path, Dr. Dougherty will introduce her most recent work in Spinal Cord Injury (SCI). Using a combination of ex-vivo electrophysiology and single-cell type manipulation in mice she will demonstrate that SCI dramatically changes the membrane properties of inhibitory interneurons in the dorsal horn that govern presynaptic gating of sensory afferent and may lead to the emergence of overt hyperreflexia. Finally, Dr. Kathe will show how a group of interneurons in the spinal cord that participate but are not critical to movement in intact mice become necessary components of motor recovery after SCI. The New Therapies Horizon builds on these insights to propose new therapies that target these single-neuron type level changes to improve behavior. Specifically, PhD-candidate Donadio will show how electrical stimulation of the primary afferents can be used to reverse the SMA-driven changes in ion channels of spinal motoneurons and significantly improve strength and fatigue in humans with SMA. Finally, Dr. Hutson will present the proof-of-concept of an optogenetic stimulation therapy that targets hyperexcitable motoneurons after SCI to treat hyperreflexia and spasticity. Discussion with the audience will focus on how single neuronal cell types shape motor behavior and if this can be leveraged to build the new therapies

Friday, May 2, 2025

08:00 – 10:00 Session 12, Panel VII

Computational mechanisms underlying contextual modulation in motor learning

Tianhe Wang¹, Apoorva Sharma², Kahori Kita³, Daniel Wolpert⁴ ¹ University of California, Berkeley, ² Yale University, ³ Johns Hopkins University, ⁴ Columbia University Discussant: Samuel McDougle

Understanding the role of context is a central issue in learning and memory. Even simple learning processes, such as classical conditioning, rely on forming associations with relevant contextual cues. Over the past 15 years, context has garnered considerable attention in sensorimotor learning research. While traditional computational approaches incorporating meta-learning mechanisms into Kalman filters and state-space models to capture some of the contextual effects, they often struggle to explain the flexibility of motor learning in diverse environments. In contrast, emerging computational methods, including hierarchical Bayesian frameworks and artificial neural networks, have successfully accounted for a broad range of phenomena in motor learning, habit formation, and decision making, substantially advancing our understanding of how context shapes learning. These advances have also fueled new research into the role of context in various motor learning processes, prompting debate on various issues such as whether different sensorimotor adaptation processes share similar contextual

modulation, whether contextual effects extend beyond basic adaptation to more complex motor skills, and what neural mechanisms underlie these contextual modulations.

This session will try to address these questions by bringing together researchers who employ a variety of behavioral tasks and computational frameworks. Wolpert will review the role of contextual inference in motor learning and show how contextual inference may underlie the differences in motor learning under distinct training curricula. He will also describe the role of visual and dynamic inputs on the way motor learning tasks are decomposed. Wang will introduce a cerebellar-like network that captures a wide range of contextual effects in implicit adaptation without relying on explicit contextual modulation. He will also present empirical findings that distinguish two distinct implicit components in sensorimotor adaptation, each displaying unique contextual sensitivities. Sharma will demonstrate how internal timing can serve as a contextual cue to separate implicit motor memories in a dual-adaptation paradigm. Kita will examine the retention and spontaneous recovery of newly learned motor skills following extended breaks, exploring how principles of contextual modulation may generalize to de novo learning. Finally, Hagura will lead a panel discussion addressing key questions, including how different processes, such as implicit recalibration and explicit aiming, are modulated by context in potentially distinct ways, and what neural mechanisms support these contextual modulations in motor learning.

10:30 – 12:30 Session 13, Individual III

OS3.2 - Determining the cognitive contributions to reduced movement vigor in people with Parkinson's disease

Jonathan Wood ¹, Amanda Therrien ¹, Aaron Wong ¹ ¹ Thomas Jefferson University Presenting Author: Jonathan Wood

Whether and how we move depends on a tradeoff between the effort required and the payoff (i.e., reward) we receive from moving. Impairment of this tradeoff has been hypothesized to underlie reduced movement vigor (i.e., bradykinesia) in Parkinson's disease (PD), although the exact nature of this disruption remains unclear. As dopamine has long been linked to reward, its reduced availability in PD could result in a devaluation of perceived reward outcomes. Alternatively, people with PD may perceive moving as excessively effortful. A third possibility is that PD disrupts the mapping between effort and reward. We assessed these alternative hypotheses in 3 separate tasks in people with PD ON and OFF their dopamine medication and compared them to matched controls. Determining the specific source of impairments in the effort/reward tradeoff is critical to understanding movement vigor more broadly and why bradykinesia arises in people with PD.

We first assessed reward perception using a standard behavioral economics task in which participants chose between a certain or risky monetary reward. Reward perception was quantified as the difference in the expected value of certain and risky choices where a person was equally likely to choose either option. Surprisingly, we found no effect of disease (PD ON vs controls p=0.59) or medication status (PD ON vs OFF p=0.36) on reward perception. Contrary to prior theories of dopamine and reward processing, this finding indicates that PD may not significantly impact the perception of reward.

Next, we assessed effort perception using an isometric force-matching task. Here, people were cued to produce a given force magnitude and then attempt to reproduce the same perceived force without cues. While everyone could accurately produce the cued forces, the reproduced forces for people with

PD were smaller than for controls (p=0.03), suggesting that people with PD perceived their exertions to be more effortful (and hence did not need to push as strongly to reproduce the perceived force). However, we did not find an effect of medication status (p=0.49), suggesting this perception is not contingent on dopamine availability.

Finally, we assessed the mapping between effort and reward by measuring participants' willingness to exert a given force for a given reward. Specifically, we quantified the change in force preference as a function of reward magnitude. While controls were willing to exert greater forces compared to people with PD regardless of reward magnitude (p=0.004), the change in force preference across rewards was similar for both groups (p=0.40) and for people with PD ON vs OFF medication (p=0.58). Thus, the effort/reward mapping was not significantly modulated by PD or dopamine. Overall, this work surprisingly hints that reward perception may not contribute to bradykinesia in people with PD. Rather, the perception of effort may play a critical, and previously underappreciated role in movement vigor.

OS3.3 - Walking toward riches: reward pays the cost of effort

Chadwick Healy ¹, Alaa Ahmed ²

¹ University of Colorado, ² University of Colorado, Boulder

Presenting Author: Chadwick Healy

Slowing of movements is a symptom of numerous motor and psychiatric disorders, yet our understanding of what determines movement speed is not well characterized. The preferred speed of walking is thought to be determined primarily by energetic cost, but can reward influence walking speed? Recent findings have shown that the speed at which we move reflects the value of what we hope to acquire in eye movements and arm reaches, suggesting a link between the neural processes that control movements and those that assign value. People reach and saccade faster to objects that promise greater reward and when there is greater opportunity cost of time. However, there is currently little understanding of how upcoming reward and a history of reward influence walking speed, a measure often thought to be prescribed by energetic cost alone.

Here, we integrate a self-paced treadmill with a virtual reality system to immerse subjects in a realistic environment that probes the effects of reward, reward history, and effort on walking speed. Sixteen subjects (n = 16; 7 Females; 22.4 ± 4.95 yrs) completed two sessions with different baseline effort conditions. In the high effort session, subjects donned a weight vest with approximately 15% of their body mass. During each session, subjects completed a series of walking trials in virtual reality that involved walking along a path collecting varied values of rewards visualized as apples. We manipulated the value of the rewards (high/10-apples, medium/5-apples, and low/1-apple), as well as the history of reward by changing the average payout of an environment. A rich environment had a higher probability of high reward (50% high, 30% med., 20% low), and a poor environment had a higher probability of low reward (20% high, 30% med., 50% low). Subjects walked at their own pace through the virtual world, where they encountered a series of rewards. Every 40 meters, a cue appeared 30 m ahead, the value of the reward was revealed after walking 10 m further, then subjects walked 20 m further to collect the reward.

Walking speeds increased as the revealed upcoming reward value increased (P < 0.0001). For the same upcoming reward value, speeds were faster in a rich environment than a poor environment (P = 0.0107). Even when the value of the reward was not revealed, subjects walked at faster speeds in a rich environment (P = 0.0119), suggesting there is an opportunity cost of time. In addition, subjects walked slower in the high effort condition versus the low effort (P = 0.0278), confirming that movement speed considers both the reward and effort of a movement rather than either one alone.

Our findings are the first to show that walking speed is sensitive to explicit reward and reward history and is modulated by effort, building on recent findings that both reward and effort can modulate movement speed. These results show significant promise that walking speed can provide a non-invasive marker of cognitive function and motivation.

OS3.4 - Reward influences movement vigor through multiple motor cortical mechanisms

Adam Smoulder ¹, Patrick Marino ², Emily Oby ³, Sam Snyder ², Steven Chase ¹, Aaron Batista ² ¹ Carnegie Mellon University, ² University of Pittsburgh, ³ Queen's University Presenting Author: Adam Smoulder

When greater rewards are at stake, humans and animals alike tend to quicken the speed and latency of movements without sacrificing their accuracy - that is, they act with enhanced vigor. How does the brain translate changes in motivation into increased movement vigor? Rhesus monkeys performed a delayed reaching task in which we cued the reward (Small, Medium, or Large) that would be given upon trial success. In population recordings from primary motor cortex (M1) and dorsal premotor cortex (PMd) we identified multiple neural correlates of motor vigor affected by reward.

First, we observed correlated effects of reward magnitude and upcoming movement vigor on movement preparatory neural activity. We identified a "vigor axis" in neural population space whereby the response of the motor cortex population correlated with movement vigor on a trial-by-trial basis. We found that greater rewards positively modulated activity along the vigor axis. We also observed that greater rewards made reach-direction conditions more separable in neural activity, and greater separability correlated with greater vigor.

Second, we found that reward facilitated the transition from preparation to movement. We calculated a neural changepoint time for each trial and saw that it decreased with greater reward. We also found that the neural speed (time derivative of firing rates) preceding movement onset was faster for greater rewards. Both of these metrics were correlated with the animals' movement vigor.

Third, we saw that reward altered neural trajectories during movement execution. Greater reward appeared to "stretch" trajectories and quicken the traversal of neural activity along them. These effects imply gain-like effects of reward on motor cortical activity, hinting at potential underlying mechanisms of the effects we observed (e.g., neuromodulatory drive).

We considered that these motor cortical correlates between reward and vigor might be driven by a single source. In this case, we would expect neural correlates of vigor to exhibit strong correlation structure themselves. Instead, we observe limited correlations between the metrics, implying multiple aspects of motor cortical activity both affect movement vigor and are modulated by reward.

Lastly, we note that when we controlled for vigor across reward conditions, we saw little-to-no impact on the ability to decode the reward cue from the neural activity. This indicates that reward effects on motor cortical activity far exceed those we would expect from reward-mediated differences in movement vigor, and that motor cortex does not simply encode reward information that is directly relevant to behavior.

We conclude that reward influences multiple aspects of motor cortical activity that relate to movement vigor, and that reward effects on motor cortex exceed those that can be explained by differences in behavior.

OS3.5 - Muscle spindles provide flexible sensory feedback for movement sequences

William P. Olson¹, Varun Chokshi¹, Jeong Jun Kim¹, Noah J. Cowan¹, Daniel H. O'Connor¹ ¹ Johns Hopkins School of Medicine Presenting Author: Dan O'Connor

Muscle spindle afferents (MSAs) are stretch-sensitive neurons that provide critical real-time feedback to the nervous system about body position and movement. While their activity is partially linked to kinematics, they are subject to complex top-down modulation during behavior. We recorded from MSAs innervating the jaw musculature (located in the mesencephalic trigeminal nucleus, MEV) in behaving mice performing a licking motor sequence task. In our task, head fixed mice licked a moving 'port' through an arc of seven locations surrounding the mouse's face to receive a water reward. The sequence progressed in opposite directions on alternating trials.

MSA ensemble activity during sequence performance was complex, evolving over single lick cycles as well as over entire licking sequences. MSAs encoded movement in a complex jaw-tongue orofacial space; while some MSAs encoded jaw movement, others were sensitive to joint conformations of the jaw and tongue. A minority of the MSAs stably encoded kinematics, and kinematics could be decoded from MSA ensembles based on this sparse population encoding. We further found that kinematics alone accounted for less than half of the total MSA spiking variability. Much of the activity was instead linked to task variables that were independent from the kinematics, including the progression of the sequence (i.e. beginning, middle, or end) as well as reward context (i.e. pre- or post-reward licking). These task related changes paralleled higher-order control signals recorded from sensorimotor cortex during this task in prior work from our group. Taken together, our work indicates that higher-order signals can dynamically tune incoming proprioceptive feedback as a mechanism for implementing flexible sensorimotor control.

OS3.6 - Understanding surprise: Dual predictive systems in whisker sensorimotor control

Ritu Roy Chowdhury ¹, Kalpana Gupta ¹, Yuyao Sun ¹, Franziska Gekeler ¹, Shubodeep Chakrabarti ¹, Cornelius Schwarz ¹

¹ Eberhard Karls University of Tübingen Presenting Author: **Ritu Roy Chowdhury**

The predictive coding framework suggests that the brain continuously generates and updates predictions to minimize sensory prediction errors, but we still don't fully understand how these predictive mechanisms relate to movement. We sought to systematically separate two systems that attenuate movement-generated sensory flow—sensory gating (SG) and state estimation (SE). We hypothesized that SG applies a broad temporal filter to movement-related sensory consequences, while SE selectively attenuates expected sensory inputs at specific times, thereby amplifying relevant inputs.

We recorded S1-spiking effects in mice performing a whisker-reach task, adapting Curtis Bell's 1981 'open-loop' paradigm from fish to mammals. First, we investigated SG's temporal profile while maintaining a fixed probability of sensory consequences. Next, we increased the probability of sensory inputs at specific time points to characterize SE-driven attenuation patterns. We show for the first time that SG peaks around movement onset, while SE disrupts this profile by producing a new peak of sensory attenuation around expected time points. Additionally, we found that SE helps to suppress whisker movements evoked by surprising sensory inputs. Optogenetic manipulations suggest that the cerebellum plays a key role in SE-induced sensory attenuation but not in the one induced by SG. Together, these findings advance our understanding of how the brain uses multiple predictive mechanisms to optimize sensorimotor control and behavior.

15:00 – 17:00 Session 15, Panel VIII

Inter-area communication for motor control

Emily Oby ¹, Matthew Perich ², Sam Snyder ³, Stefan Lemke ⁴, Maureen Hagan ⁵ ¹ Queen's University, ² Université de Montréal, ³ University of Pittsburgh, ⁴ University of North Carolina, ⁵ Monash University Discussant: Emily Oby

Motor control is remarkable in its flexibility- allowing us to perform a wide range of complex movements, adapt to new tasks, and choose appropriate action for a given context or environment. The brain achieves this flexibility, at least in part, through the dynamic interactions between distinct brain areas in the sensorimotor loop. From the sensory cortices processing incoming information, to the motor areas executing precise movements, and the higher-order brain areas responsible for planning and decision-making, each area interacts and communicates with other areas in order to orchestrate the movement. How is communication instantiated and modulated across brain areas to allow for flexible motor control? In this session, we will explore recent work that examines how the sensorimotor brain areas coordinate and communicate their activity, enabling flexible and precise motor control.

Neural communication must be dynamic and flexible in order to guide behavior. Matt Perich will explore methods to estimate principles of inter-areal communication and demonstrate that transient interactions between sensory and motor areas can enable flexible behavioral output.

Behavioral tasks like eye-hand movements engage brain areas across networks to coordinate behavior and can allow us to study neural mechanisms of communication across brain areas. Maureen Hagan will show how the temporal patterns of neural activity across areas is modulated by behavioral demands and may be a signature of inter-area neural communication.

Precise, genetically-defined manipulators of cortical, subcortical, or cerebellar areas can each disrupt skilled motor control in rodents. However, the manner by which these distributed areas may interact to control skilled movements remains unclear. Stefan Lemke will present evidence that the strength of cross-area coordination captured from large-scale neurophysiology during motor control covaries with the ability to perform skilled movements in genetic mouse models with typically and atypically developed nervous systems.

Finally, Sam Snyder will share a causal test of the flexibility of interactions between primary motor (M1) and premotor cortex (PMd). Using a brain-computer interface task designed to challenge monkeys to break observed correlations between M1 and PMd, he will show that inter-area interactions are more flexible than within area interactions.

Together this panel will highlight the importance of understanding how distinct populations of neurons interact and communicate to plan, execute, and learn new movements. The discussion will focus on our understanding of how the brain flexibly controls movement and if this can shed light on how disruptions to the sensorimotor neural networks might contribute to motor impairments.

17:00 – 18:00 Distinguished Career Award Presentation and Talk

Notes from the Underground: Psychological Perspectives on Cerebellar Function Richard Ivry, University of California, Berkeley

The cognitive neuroscience revolution provided a new theoretical framework for using the tools of neuroscience to study the mind. Central to this paradigm shift was the idea that the focus of our analysis should be on the component operations underlying task domains rather than on the tasks themselves. I will provide a retrospective on our efforts to apply this strategy to motor control, and in particular to develop a functional account of the role of the cerebellum in coordinated movement, sensorimotor learning, and cognition. Using simple model tasks, the behavioral analysis of healthy individuals and patients with cerebellar disorders has provided insight into unique computational characteristics of this subcortical structure. Prominent among these is the idea that the cerebellum is critical for tasks that require the precise representation of temporal information. This hypothesis places an important constraint on the predictive capacity of the cerebellum, providing an account across a range of task domains of conditions that are cerebellar dependent and, as important, conditions that are cerebellar independent. These dissociations are essential for building a psychological level account of how the cerebellum supports coordinated movement and thought.

Poster Session 1

A – Control of Eye & Head Movement

1-A-1 - Simulation of bilateral control of horizontal saccades in mTBI

John Anderson¹

¹ University of Minnesota

<u>Details</u>

Mild traumatic brain injury (mTBI) can result in significant deficits affecting vision and eye movements, including vergence, saccades, pursuit, and the vestibulo-ocular reflex [Hunfalvay et al. (2019). Concussion, 4(1); Crampton et al (2021). Brain Injury, 35; McDonald et al. (2022). J Ey Mov Res, 15(2)]. These issues can result in problems with balance, eye-head coordination, and visual-motor transformations underlying goal-directed movements. The deficits can occur after multiple head trauma events, and in some cases after a single mild TBI event. The symptoms can persist for years after the original trauma [4], and become progressively worse over time. The general aims for this research are to characterize, in mTBI, the coordinated movement of the two eyes during changes in gaze in response to 3D movements of a visual target and to gain insight into underlying oculomotor control problems. Our recent work has identified significant differences in the time courses of right and left eye movements during horizontal saccades. One pattern shows a difference in right vs. left eye velocity during the acceleration phase of a saccade and the opposite (for right vs left eye velocity) during the deceleration phase of a saccade. Other patterns include different velocities for adduction vs. abduction and right vs. left eye that is similar during both acceleration and deceleration. Simulations of a bilateral parametric model for oculomotor control signals suggest different pathologies that might involve the brainstem burst neurons, cerebellum, and oculomotor pathways. In combination with other oculomotor variables, quantification of a binocular disparity in eye velocity during saccades might help with identifying mTBI.

1-A-2 - Handedness modulates visual attention during bimanual reaching

Florian Kagerer¹, Faith Houck¹

¹ Michigan State University

Details

Research on visually guided bimanual reaching has mostly focused on hand kinematics, but little is known about how visual attention is allocated between the two hands. This exploratory study investigates gaze behavior during bimanual reaching tasks of varying complexity, and the influence of each hand's differing control strength on visual attention.

12 right-handed (avg. 21 yrs; 9 females, G1) and 12 left-handed participants (22 yrs; 10 females, G2) performed bimanual reaches, using two joysticks each controlling a cursor. Cursors and targets (r=0.5 cm) were displayed on a monitor 60 cm in front of the participant.

There were three experimental conditions: Baseline (BLN, 10 trials), where the cursors had to be moved from two home positions (17 cm apart) to two targets straight ahead at 90 deg. In an isodirectional condition (ISO, 20 trials) the cursors had to be moved from the home positions to two targets located at either 30 or 150 degrees; both hands always moved in the same direction. Lastly, an an-isodirectional condition (ANI, 20 trials) with the same target locations, but with the hands moving in mirror-fashion, either to the lateral or medial targets; movement amplitude was 7.5 cm.

Eye movements were recorded at 120 Hz using a Tobii Pro Fusion eye tracker. A chin- and headrest supported the participants' heads. Trials started with a center fixation cross which disappeared when the targets appeared; participants were then free to direct their gaze wherever necessary. Eye movements were classified using the modified Nyström & Holmqvist algorithm (Friedman et al, 2018), with a minimum fixation duration of 40 ms. Eye movements were analyzed for the period between hand movement onset and offset.

Variables of interest were the sum of fixation dwell time in regions of interest (ROIs) around each target, and the first ROI fixated upon as a percentage of trials. For the ISO and ANI conditions, effects of movement direction (medial/lateral) on gaze, in addition to hand (dominant/nondominant) were analyzed by 2(group) x 2(dominance) x 2(direction) ANOVAS.

We found that in BLN, G1 spent more time fixating on the nondominant left hand, whereas G2 looked more at their dominant left hand; there were no group differences as to which target was looked at first. In ISO, both groups spent more time looking at the medial ROI of their dominant hand, and particularly G2 looked at the dominant hand and the medial ROI first. In ANI, again both groups looked more at the dominant hand they both looked at the dominant hand first.

The findings suggest that 1) visual attention allocation during bimanual reaches is influenced by the different control strengths for each hand, with the non-dominant hand's accuracy control strength requiring less attention than the dominant hand; 2) targets toward the body midline appear to require more visual guidance, possibly related to the higher control complexity for movements towards the contralateral side of the body.

1-A-3 - Cell types and priors: Cerebellar encoding of sensorimotor timing

Julius Koppen¹, Ilse Klinkhamer², Marit Runge¹, Devika Narain¹

¹ Erasmus University Medical Center, ² Erasmus Medical Center

Details

Behavior in the natural world is rife with feats of temporal precision but laboratory measurements of such behaviors reveal surprising biases in sensorimotor timing. Previous theoretical work attributes some of these biases to Bayesian inference processes that increase their reliance on prior knowledge of well-timed movements under uncertainty. We, however, know little about how neural circuits utilize prior knowledge required for precise temporal control of movements. Here we use theory, large-scale electrophysiology, machine learning, and optogenetics to investigate whether cerebellar circuits could provide a substrate for encoding prior knowledge of temporal statistics to generate precise movements. We train mice on a modified eyeblink conditioning task, where they learn associations between a visual cue (conditioned stimulus, CS) and a periocular airpuff (unconditioned stimulus, US). Unlike conventional eyeblink conditioning, the time intervals between the CS and US are drawn from discrete uniform probability distributions of different statistics, i.e., very narrow, narrow, and wide. After several pairings, the eyelid learns to close predictively and on test trials where the airpuff is omitted, we evaluate the statistics of the predictive (conditioned) eyelid closure for different prior distributions. We found that kinematic and temporal properties of the eyelid movement adapted to changes in the statistics of the stimuli. Neural activity profiles of cerebellar Purkinje cells and putative molecular layer interneurons recorded during behavior in lobules IV/V and Simplex of the cerebellar cortex concomitantly changed their statistics to accommodate the changing prior distributions. We used recent deep-learning techniques to identify cerebellar cell-types and to decode trial-by-trial activity from cerebellar cortical neurons. We also analyzed latent population dynamics for different prior distributions to conclude that neural population tuning changes its statistics when the prior distribution switches from narrow to wide. Calibrated optogenetic perturbations to cerebellar Purkinje cells within the duration of the temporal distribution caused a complete suppression of the prior-related response. Furthermore, we found prior-related signaling in cerebellar Purkinje cell complex spike activity that was time-locked to the onset of prior distributions. Finally, we propose a computational model of the cerebellar-olivary circuit that uses juxtaposed plasticity principles to explain how the cerebellar cortex encodes and leverages prior knowledge to generate precise eyelid control.

<u>1-A-4 - Spatially uninformative sounds modulate midbrain visual activity with and without primary</u> <u>visual cortical input</u>

Tatiana Malevich ¹, Matthias Baumann ², Yue Yu ², Tong Zhang ², Ziad Hafed ³

¹ University of Tübingen, ² Hertie Institute for Clinical Brain Research, ³ Centre for Integrative Neuroscience

<u>Details</u>

We recently discovered that spatially uninformative sounds can activate otherwise dormant visualmotor pathways bypassing the primary visual cortex (V1) (NCM 2024). Here, we aimed to better understand how this might happen. We recorded from superior colliculus (SC) neurons (two monkeys) with either intact or focally inactivated V1 (muscimol microinjection; 1.5-2.5 μ L; 10 mg/1mL). We presented a 0.2 deg radius disc within the neurons' receptive fields (RF's) and randomly interleaved trials in which we paired the visual stimulus onset with a bilateral sound pulse (50 ms; 1 kHz). This sound pulse was neither informative about the visual stimulus location nor spatially aligned with RF locations. In the first set of tasks, monkeys were instructed to fixate at the center of the screen and ignore the stimuli. With intact V1, SC neurons showed little, if any, responses to the sound alone. Nonetheless, visual response strength and latency were diversely affected (sometimes being stronger and earlier for the vision+sound trials, other times being weaker and later, and yet other times being unaffected). Such multisensory integration was also evident in local field potentials (LFP's), with evoked responses to multisensory stimuli being enhanced and distinct from those elicited by unimodal stimuli in either modality. With inactivated V1, SC visual responses were much sparser, both at the single unit and LFP levels. However, adding spatially uninformative sounds unmasked a relatively weak visually-evoked LFP response that was not explained by sound-only responses. Interestingly, these effects were drastically amplified in an active oculomotor task, where monkeys executed guessed, visually guided foveating saccades toward the visual target. With intact V1, some SC neurons exhibited clear auditory responses to sound alone, and multisensory integration was evident in both visual and motor SC responses. Notably, V1 inactivation abolished most – but not all – SC visual responses, even to unimodal visual stimuli. At the same time, some neurons displayed visual tuning properties when sound was added to the visual stimulus. Moreover, despite the loss of V1 input, SC motor responses retained their visually-driven sensory tuning properties, which were also modulated by the presence of the sound. Finally, we sampled some inferior colliculus (IC) neurons. With intact V1, when IC neurons exhibited visual responses, they showed clear multisensory integration, even without having sound-only responses; however, LFP visually-evoked responses were predominantly driven by sound. With inactivated V1, IC single-unit and LFP responses were abolished. These results underscore the distinct SC and IC roles in multisensory integration, and they support a potential SC involvement in visually-guided behavior when V1 is compromised.

1-A-5 - Spontaneous recovery of saccadic adaptation explained by a postdictive model

Max Johann Schuhriemen¹, Jana Masselink², Markus Lappe²

¹ University of Münster, ² University of Muenster

Details

Adaptation of saccadic eye movements is induced by stepping the target during movement execution, hence producing a targeting error. It results in a systematic lengthening of the saccade in response to outward target steps and shortening in response to inward target steps. Spontaneous recovery is a nonlinear phenomenon in which an initially learned system state is extinguished but later re-emerges in a seemingly neutral situation.

Traditionally, spontaneous recovery has been explained by models that rely on motor changes driven by sensory prediction error. However, when motor changes are considered alongside accompanying changes in visual target localization, Masselink \$\&\$ Lappe (2021) have shown that saccade adaptation cannot be explained by sensory prediction error. Instead, they proposed a model that adapts visual, otor and internal saccade gains driven by postdictive motor error. To investigate whether the postdictive error-based model can also explain spontaneous recovery, we simulated different scenarios in which spontaneous recovery occurs. Our modeling results show that spontaneous recovery can be observed when adaptation of the internal saccade gain is accelerated in the extinction phase. Hence, the internal saccade representation decouples from the actually performed saccade , producing a postdictive motor error that drives spontaneous recovery after extinction. This results in spontaneous recovery, both in the saccade amplitude and in post-saccadic target localization. Our findings suggest that spontaneous recovery emerges naturally within the postdictive framework when learning rates for visual, motor and internal saccade gains dynamically adjust to changes in the experimental context.

1-A-6 - Dark contrasts are immune to saccadic suppression in the primary visual cortex

Wenbin Wu¹, Yue Yu¹, Tatiana Malevich¹, Matthias Baumann², Tong Zhang², Carlotta Trottenberg¹, Ziad Hafed³

¹ University of Tübingen, ² Hertie Institute for Clinical Brain Research, ³ Centre for Integrative Neuroscience

<u>Details</u>

Saccade generation is accompanied by a dramatic reduction in perceptual sensitivity for perimovement stimulus onsets, which also affects subsequent saccade efficiency. Neuronal correlates of this phenomenon have been observed in multiple brain areas, including the retina, superior colliculus (SC), and primary visual cortex (V1). However, how each area specifically contributes to the perceptual effect itself remains unknown. Here, we were motivated by previous observations that perisaccadic perceptual detectability is similarly impaired for dark and bright stimuli, and that this is also true in the SC (Wu & Hafed, 2024). We asked whether these observations are universal (and thus observable in other brain areas), or whether they reveal a particular role for the SC in mediating them. We recorded from 248 SC neurons (three monkeys) and 325 V1 neurons (two monkeys). In each trial, a disc (0.51 deg radius; bright or dark) appeared within the recorded neurons' response fields. We measured stimulus-evoked visual response strength as a function of stimulus onset time relative to microsaccades. In the SC, we replicated the earlier observations (Wu & Hafed, 2024) that suppression strength is similar for darks and

brights. Surprisingly, this was not the case in V1: all of our dark contrasts were completely immune to saccadic suppression. Moreover, bright contrasts underwent weaker suppression than in the SC. These results suggest that perisaccadic perceptual detectability (similarly suppressed for darks and brights) is not mediated by V1. However, this does not mean a complete lack of V1 impact on perisaccadic vision. In five human subjects, we repeated the same experiments but now presented supra-threshold oriented bars (either dark or bright). The bars (at 20% contrast) were perisaccadically detectable in 100% of the trials. Nonetheless, orientation discrimination thresholds were still elevated, but only for the bright stimuli. Thus, there is a highly selective saccadic suppression of exclusively ON processing pathways in V1.

B – Fundamentals of Motor Control

<u>1-B-7 - Transmission of Cortical Beta-Band Oscillations to a motor neuron pool is uniform and independent of motor neuron size</u>

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Details

Beta oscillations (13–30 Hz) are a prominent neural rhythm observed in the sensorimotor cortex and are associated with steady motor states and sensorimotor integration. These oscillations propagate from the cortex through the spinal cord to motor neurons and, ultimately, to muscles. Previous research suggests that this transmission primarily relies on the fastest corticospinal fibers during light force contractions. However, these findings were limited to low-threshold motor units, leaving open the question of whether the same pathway operates across varying contraction levels.

We characterized beta-band projections to the motor neuron pool of the tibialis anterior across increasing force levels. Twelve subjects performed ankle dorsiflexion at six target forces (5%, 10%, 20%, 30%, 50%, and 70% MVC) while EEG and high-density EMG were recorded. Motor unit firing patterns were decomposed from high-density EMG, and their activity was summed to compute the cumulative spike train, providing a partial estimate of the neural drive to the muscle. As contraction levels increased, larger motor units were progressively recruited, following the size principle. Corticomuscular coherence analysis revealed that beta-band transmission remained constant across contraction levels, indicating that beta oscillations project similarly to the muscle regardless of motor neuron size. To further investigate this projection, we estimated corticospinal transmission delays using the cumulant density function, which identified peak correlations between cortical and muscular activity. The mean delays ranged from 25.99 ± 3.24 ms at 5% MVC to 22.29 ± 2.29 ms at 70% MVC, with intermediate values of 26.16 ± 3.36 ms (10% MVC), 24.17 ± 3.54 ms (20% MVC), 22.77 ± 3.61 ms (30% MVC), and 21.49 ± 3.16 ms (50% MVC). Using an average axon length of 500 mm and peripheral conduction velocities from 41 to 57.5 m/s, we estimated motor neuron transmission delays from 12.2 ms (low-threshold motor neurons) to 8.7 ms (high-threshold motor neurons). These values fully explain corticomuscular delay variations, combining a ~14 ms corticospinal delay with conduction-dependent peripheral delays. These delays are compatible only with the fastest corticospinal fibers, reinforcing prior findings.

These results indicate that corticospinal fibers conveying beta oscillations engage all motor neurons uniformly, operating at the minimal delay imposed by the fastest conduction pathways at the spinal level. This finding advances our understanding of beta-band corticospinal transmission and its role in motor control.

1-B-8 - Influence of uncertainty on preparatory activity in motor cortex during reaching

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Details

In our daily lives we are constantly forming and correcting motor plans to flexibly interact with the external world. Often times the information available during the process of planning is incomplete, thereby causing uncertainty about the movement goal. It is unclear how the motor system prepares movements under different levels of uncertainty, and how this uncertainty affects the ability to reprepare movements. Using a forced reaction-time paradigm, a rhesus macaque was trained to produce center out reaching movements to one of two diametrically opposing potential targets. In this task, a timing cue flashed three times in succession (500 ms between flashes). The third flash was the go-cue, and the monkey had to launch the movement coincident with it (within 100 ms). The two potential targets were displayed at the time of the first flash and then disappeared. The actual target was then displayed at varying times prior to 'forced' movement initiation at the go-cue. We manipulated uncertainty about the target location using a coloring scheme that indicated the probability (p) of where the final target would appear. For example, when both potential targets were white, p = 0.5, the final target could appear at either location with equal probability. When the time between actual target display and movement onset was briefer than typical visual processing time (~ 100 ms), the monkey had to 'guess' the location of the target. In these cases, and when guessed incorrectly, the monkey corrected the movement midstream. We found that the monkey was able to re-prepare movements faster with increasing levels of uncertainty. While the monkey performed this task, we recorded 202 neurons from the dorsal pre-motor and primary motor cortex. During the preparatory period, we observed a graded reduction in the distance between neural states for the two potential movements with increasing levels of uncertainty. Such an outcome in neural state-space could theoretically explain the faster repreparation times under higher levels of uncertainty. Importantly, the different preparatory states still led to highly similar population dynamics during movement execution. Furthermore, we also found a dimension in neural state-space that separated the neural states based entirely on the level of uncertainty during both movement preparation and execution. Whether this dimension overtly represents uncertainty is an open question. Overall, these results provide insight on the structure of neural population activity in the motor cortex while preparing and executing movements under conditions of uncertainty.

1-B-9 - Planning while moving: when two hands are better than one

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¹ Université de Sherbrooke, ² CNRS, Université de Poitiers, Université de Tours, CeRCA

<u>Details</u>

We are routinely confronted with situations in which, while already being engaged in an action, we need to plan the following action. As a result, ensuring adequate planning while moving is key for many everyday tasks. Because there is growing evidence that planning and performing an action might rely on (partly) shared neural substrates, we wished to examine the extent to which the planning of an upcoming movement depended on whether the same limb was already engaged in an action. To achieve this, we designed a 2-choice reaction time (RT) task in which participants (N=24) had to move their

dominant hand rightward or leftward following a go signal. In some of the experimental conditions, the required side was precued a few seconds before the go signal, thus disambiguating the direction of the upcoming hand movement. When that task was performed with the hand immobile before the go signal, the provision of the precue shortened RT by 44ms (-15%) as compared to a no precue condition, an observation consistent with the fact that participants preprogrammed some aspects of the future action. However, when participants had to perform the same task on top of a background rhythmic (forward-backward) movement of the same hand, the benefit provided by the precue dropped to 16ms (-5%) suggesting a lesser capacity to preprogram the reaching movement. In a follow-up experiment with new participants (N=24), we sought to determine whether the effect of the precue would be weaker if the rhythmic movement was performed by the contralateral (non-dominant) hand while still performing the RT task with the dominant hand. Consistent with the first experiment, we found that when the RT task was performed with both hands at rest, the provision of the precue strongly shortened RT (47ms or -15%). However, in contrast to the initial experiment, the rhythmic movement of the contralateral hand did not weaken the effect of the precue on the RT of the dominant hand, which was reduced by 38ms (-11%). Altogether these results confirm that planning and executing an action are neural processes that can simultaneously coexist but are not fully independent. The fact that reduced interference was observed when moving and planning engaged separate limbs can be interpreted as evidence of a motoric bottleneck at the hemispheric level.

<u>1-B-10 - Neural encoding of action intention and observation in human motor and posterior parietal</u> <u>cortex: insights from intracortical recordings in tetraplegic participants</u>

Vasiliki Bougou ¹, Jorge Gamez ², Emily Rosario ³, Charles Liu ⁴, Kelsie Pejsa ², Ausaf Bari ⁵, Richard Andersen ²

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<u>Details</u>

Despite extensive electrophysiological recordings in nonhuman primates and imaging in humans, the neural mechanisms underlying action observation and recognition in humans remain unclear. We recorded neural activity during action intention and observation in two tetraplegic participants implanted with intracortical arrays: N1 (96-channel arrays in motor cortex [MC] and superior parietal lobule [SPL]) and N2 64-channel arrays in medial MC (MCM), lateral MC (MCL), supramarginal gyrus [SMG], and superior parietal lobule [SPL]. Participants performed (1) an observation task, where they viewed videos of a left or right hand performing three object manipulations (rotation, lift, slide) in two directions (left, right), and (2) an intention task, where a cue specified the hand and manipulation to be attempted. Neural activity was recorded over three sessions per participant (total active channels: in N1 MC: 271, SPL: 236; N2: MCM: 256, MCL: 275, SMG: 168, SPL: 262). We identified brain regions involved in action intention and observation by measuring responsive sites (p < 0.05, 1 - way ANOVA compared to baseline). More intention responses were found in MC (N1: 104; N2: MCM: 115, MCL: 104), in SPL (N1: 54; N2: 109), and less in SMG (N2: 36). Observation responses were limited in MC and SMG (N1: MC: 23; N2: MCM: 48, MCL: 35, SMG: 14) but strong in SPL (N1: 42, N2: 99 sites). A three-way ANOVA revealed that during intention MC is primarily involved in effector encoding (N1: 22 sites, N2: MCM: 62 sites, MCL: 30 sites), while SPL encodes action type (N1: 40 sites, N2: 20 sites) and effector (N2: 14 sites). SMG had limited tuning (5 sites for effector and action type). During observation, SPL exhibited the strongest tuning for action type (30 sites). Decoding with linear discriminant analysis supported these

findings. During intention, both MC and SPL (N1, N2) exhibited robust decoding of action type (N1: MC: 58.3%, SPL: 68.5%; N2: MCM: 59.7%, MCL: 61.1%, SPL: 78.5%) and effector (N1: MC: 83.9%, SPL: 76.3%; N2: MCM: 92.5%, MCL: 89%, SPL: 86.8%), while direction was largely undecodable. During observation, only SPL (N1, N2) achieved above-chance decoding, with SPL in N2 showing the highest accuracy for action type (80.4%). Cross-decoding showed that training on observation and testing on intention worked in both MC and SPL (N1, N2). However, observation-to-intention decoding was only successful in SPL. Our results show that MC exhibits explicit representations during action intention, meaning the features are directly decodable, but not during observation. However, successful cross-decoding from observation to intention reveals a shared latent structure, suggesting that observation signals are weaker representations of intention signals. In contrast, SPL shows explicit representations in both intention and observation, with directly decodable features, supporting bidirectional decoding and a structured mapping between observed and intended actions.

<u>1-B-11 - Hand dominance influences Spatiotemporal finger coordination in precision grip, not finger</u> <u>individuation</u>

Charisma Byrd ¹, Timothy Ma ², Divya Rai ¹, Jeremy Brown ³, Jing Xu ⁴

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Details

The ability to execute complex, precise hand movements is a hallmark of human dexterity. Handedness—the consistent preference for using one hand over the other—has traditionally been defined by preference (Corey et al., 2001), skill (Annett, 1970; Flowers, 1975), or strength (Chau et al., 1997); however, this semantic ambiguity underscores the need to investigate its influence on fine motor control. While minimal literature reports hand dominance differences in individuated finger movements (Abolins and Latash, 2021) dexterity asymmetries appear more pronounced in tasks requiring multiple finger coordination, e.g., found in thumb-to-finger opposition (Reilly and Hammond, 2004). Here, we investigate the effect of hand dominance on both finger individuation and precision grip using a novel hand device with highly sensitive 3D isometric fingertip force measurements (Xu et al., 2023). We hypothesized that (1) finger individuation ability is not shaped by handedness and (2) spatiotemporal coordination across multiple effectors, crucial for precision grip ability, is the key feature that distinguishes the superior dexterity in the dominant hand.

Methods: Participants completed finger individuation and precision grip tasks using a virtual environment. The individuation task required force generation with an instructed finger in six 3D directions while keeping the non-instructed fingers inactive. The precision grip task involved thumb-to-finger opposition to grasp a small object in the virtual space with a high demand for accuracy. Three separate experiments evaluated individuation (Exp 1: n=16, 20 ± 1.46 years, 15 right-handed, 12 female), precision grip abilities (Exp 2: n=22, 24 ± 5.55 years, 22 right-handed, 10 female), and both across hands (Exp 3: n=10, 21 ± 2.52 years, 9 right-handed, 7 female), with handedness assessed via the Edinburgh Handedness Inventory. Finger individuation was quantified using a 3D Individuation Index (Xu et al., 2023), while precision grip performance was assessed using grip angle, touch desynchronization, and force trajectory synchronization. Linear mixed-effects models were used to analyze dexterity measures, accounting for within-subject variability where appropriate.

Results: Significant handedness effects were observed in precision grip, particularly in touch desynchronization (Exp 2: p=0.007; Exp 3: p=0.02) and trajectory synchronization (Exp 2: p=3.72e-09; Exp 3: p=0.005), suggesting that handedness influences multiple finger coordination. Grip accuracy

differed between hands for Experiment 2 (p=0.005) and not for Experiment 3 (p=0.82). No handedness effects were found in finger individuation from both Experiments 1 and 3 (all p > 0.05), aligning with prior literature. Conclusion: The results suggest hand dexterity asymmetries primarily emerge in tasks requiring precise spatiotemporal coordination rather than tasks focused on isolated finger control.

<u>1-B-12 - Single-neuron and population approaches reveal spatially structured neural dynamics across</u> <u>frontal motor cortex</u>

Ryan Canfield ¹, Tomohiro Ouchi ¹, Leo Scholl ¹, Pavithra Rajeswaran ¹, Lydia Smith ¹, Amy Orsborn ¹

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<u>Details</u>

Brain-computer interfaces (BCI) directly translate neural activity into the control signals for an external device. BCI performance depends on the ability to measure neural activity that contains movement-related information. Past work primarily used microelectrode arrays with pre-defined geometry, targeting them to general regions known to relate to movement like the primary motor cortex (M1). Advanced sensor technologies open new possibilities for more flexible, targeted recordings, which raises new questions about how to optimize sensor placement for movement decoding. Anatomical and multineuron mapping studies suggest that movement information is not homogeneously distributed across frontal motor cortices. Population-level perspectives have improved decoding by leveraging structured neural dynamics, yet the relationship to spatial structure at the anatomical level remains unclear. Insights into how information is distributed across frontal motor cortices, both at the single neuron and population level, will improve our ability to maximize movement decoding.

To address this, we made spatially precise recordings across the motor cortical surface using highdensity laminar microelectrode arrays (Neuropixels) (Fig. 1a). We collected data from two monkeys while they performed a well learned center-out reaching task. This allowed us to map functional contributions to movement decoding across 3 spatial dimensions throughout a large area of frontal motor cortices. We assessed how the recorded units contributed to movement and their dynamics, depending on their location, at both a single-unit and population level.

Consistent with prior mapping studies, we found spatially localized clusters of units that were predictive of target direction. These clusters were non-uniformly distributed across the surface of the brain and in depth. Interestingly, we found that the location of the clusters on the cortical surface could be predicted by surface activity (μ ECoG) recorded from the same monkeys while performing the same task (Fig 1b). We then leveraged Canonical Correlation Analysis (CCA) to investigate the similarity of population-level dynamics across the cortical surface. We found that neuronal clusters across the caudal regions (M1) in the chamber produced similar dynamics. However, neurons recorded in rostral parts of the chamber (pre-motor cortex; PMd) produced different activity patterns to neuronal populations recorded in other parts of PMd and in M1 (Fig. 1c).

These results suggest that a network of neuronal clusters that encode this reaching behavior likely exists within the frontal motor cortices. The clusters involved in this network are spatially distributed across the cortical surface, but their location can be predicted by multi-neuron mapping modalities such as μ ECoG. Mapping tools with high-spatial resolution will likely be a valuable tool for guiding sensor placement and enable precise network-specific targeting to improve BCI performance. This data set provides unique opportunities to connect the single-unit and population dynamics, which will likely provide insights into how networks of neurons coordinate to produce movement.

1-B-13 - Differential muscle activation corresponds to similar movements in walking Drosophila

Raveena Chhibber¹, Lili Karashchuk², Chris Dallmann³, Elliott Abe¹, John Tuthill¹, Bing Brunton¹

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<u>Details</u>

For many animals, legged locomotion is crucial for survival in unpredictable environments. In order to move limbs, premotor circuitry drives activity in motor neurons, activating muscles for contraction. Recent structural analysis of premotor circuit connectivity in the fly has shown that leg motor neurons cluster into non-overlapping modules driving muscle activity. However, the temporal dynamics and functional role of these muscles during walking remains poorly understood.

Here, we leverage the genetic toolkit of the fruit fly with robust 3D joint tracking to understand how premotor circuits generate leg kinematics. We used wide-field fluorescence imaging to measure muscle calcium activity in two antagonistic shoulder muscles during walking—the swing muscle and the stance muscle. When the fly was turning, we found relative changes in the phase of calcium activity between the two muscles correlated with left and right turns, where larger shifts correlated with larger turns.

Unexpectedly, during forward walking, different muscle activity patterns corresponded to indistinguishable kinematics. Specifically, the swing muscle was consistently recruited before the onset of swing, whereas the stance muscle was activated in-phase, non-phasically, or anti-phase with the swing muscle, resulting in three distinct muscle coordination patterns. Interestingly, our analysis showed that flies do not transition between coordination patterns on a step-by-step basis–rather, the relative activity of the swing and stance muscle changes gradually over many steps.

To better understand how and when flies change muscle coordination patterns during walking, we fit a Markov model to estimate a per-step transition probability between coordination patterns. Interestingly, our analysis found that flies do not transition between coordination patterns on a step-by-step basis—rather, they transition gradually over many steps.

We thus propose that swing muscle contraction inextricably drives forward leg movement at a fixed phase within the step cycle, while the timing of stance muscle activity fine-tunes force production to maintain consistent leg trajectories. Together, our results suggest that fruit flies may take advantage of this complex interaction between activity and movement to walk through challenging and rugged environments.

We are now leveraging a connectome dataset of premotor circuit connectivity to understand how neural circuits implement the flexible control of antagonistic muscles. We plan to use these measured muscle activity dynamics to uncover premotor circuits modulating the drive to antagonistic muscles, allowing us to perturb circuits that support specific behaviors.

<u>1-B-14 - Short trains of transcutaneous vagus nerve stimulation increase pupil size and online</u> <u>measurements of corticospinal excitability</u>

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<u>Details</u>
Transcutaneous vagus nerve stimulation (tVNS) shows promise as a method to better understand human behaviour and treat neurological disorders. tVNS involves the application of electrical simulation to the auricular branch of the vagus nerve via the cymba conchae in the ear. Effects are typically compared to a sham stimulation condition in which electrical stimulation is applied to the ear lobe. tVNS elevates arousal, as evidenced by increased pupil size, heart rate, and skin conductance. These changes in arousal markers are thought to result from stimulation spreading from the vagus nerve to the locus coeruleus (LC), which delivers noradrenaline to the cortex via broad reaching projections.

While the effect of tVNS on traditional markers of arousal are reasonably well defined, less is known about how tVNS alters corticospinal excitability, as assessed by applying single pulses of transcranial magnetic stimulation (TMS) over the primary motor cortex (M1). This is particularly the case for "online" effects, i.e., effects while tVNS is active. To address this, we elicited motor evoked potentials (MEPs) in the right flexor dorsal interosseous at 8 timepoints relative to the onset of 4 second trains of tVNS and sham stimulation (-1s (baseline), 0.2s, 1s, 2s, 3s, 4 s, 5s, 6s). Twenty MEPs were collected per condition. Pupil size was concurrently recorded during each TMS trial, as well as during 80 "noTMS" tVNS and sham trials. Trial types were randomly interleaved in 10 blocks of 40 trials.

In line with previous investigations, tVNS increased pupil size relative to sham stimulation, with significant differences emerging from 1.2s to 4s after tVNS onset, and peaking at 1.6s. For corticospinal excitability, tVNS also increased the peak-to-peak amplitude of MEPs relative to sham stimulation. Specifically, significant differences were observed at 1s (10% increase), 2s (11% increase), and 3s (14% increase) post tVNS onset.

To our knowledge, this work represents the first evidence that short trains of tVNS drive "online" increases in corticospinal excitability. The effect of tVNS on corticospinal excitability differed somewhat from pupil size, with the onset of the increase occurring slightly earlier for MEPs and the peak occurring ~ 1.5 seconds later than in pupil size. While previous studies have focused on examining the effects "offline" after an extended bout of tVNS, our results suggest that to properly understand the relationship between tVNS and corticospinal excitability, it may be necessary to acquire measurements "online" while tVNS is active. Pairing tVNS with online corticospinal excitability measurements in this manner further opens the possibility for investigating LC-M1 circuit dynamics during behavioural paradigms.

1-B-15 - Keeping track of objects in real and virtual environments

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<u>Details</u>

Interacting with the world requires us to localize objects and to keep track of where they are in space. This task can be accomplished by the combination of different spatial reference frames, i.e. egocentrically, by encoding objects relative to the self, and allocentrically, by encoding objects relative to other objects or landmarks in the environments (e.g., room corners). Spatial coding plays an essential role for perception and action and has been shown to be affected by multiple low-level perceptual and high-level cognitive factors, such as spatial proximity or the task relevance of landmarks. In my talk, I will present the behavioral findings from two studies which looked at the influence of egocentric and allocentric cues in spatial encoding of objects in the real world and naturalistic virtual environments. First, I will show results on how people encode, store and recall object locations for action and how these processes are influenced by scene semantics. In virtual reality, we varied the semantic relationship between small, local objects and contextually-related anchor objects to determine the role of scene semantics on allocentric coding for actions. After scene encoding and a short delay participants were asked to place one of the previously seen objects back to its original position. During the delay and unnoticed to the participant one of the anchor objects was shifted to the left or right. We found systematic shift effects indicating that anchor objects were used as effective allocentric cues. However, these effects were independent of semantic congruency. Second, I will focus on the spatial encoding and updating of object positions in situations where the orientation of the entire room changes. To this end, we misaligned the virtual room (pitched up or down) with respect to the real room and asked participants to point to targets in one of the two environments. We observed a strong reliance on allocentric cues irrespective of whether participants encoded the target positions in the real world and pointed to their remembered location in virtual reality, or vice versa. Overall, our results show that people strongly rely on allocentric cues when encoding and updating objects for goal-directed actions, leading to systematic biases in space perception and action. These results also have implications for personal safety when navigating in virtual reality and real world environments.

<u>1-B-16 - Reward and effort levels modulate phase-amplitude coupling and granger causality within and</u> between the sensorimotor cortices before movement planning

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Details

Reward and physical effort expectations are crucial in motor control and decision-making. While previous studies have demonstrated that subcortical regions encode expected reward and effort costs, little is known about how sensorimotor cortices (S1, M1, PMd) integrate these factors before movement planning. This study investigates how local field potentials (LFPs) in these cortical areas are modulated by the expected reward and effort levels, with a focus on Phase-Amplitude Coupling (PAC) and Granger Causality (GC) as indicators of intra- and inter-cortical connectivity.

A rhesus macaque was trained to perform a center-out reaching task in three conditions: (1) rewardonly, (2) effort-only, and (3) combined reward-effort, where visual cues indicated future reward magnitude (R1-R3) and effort level (E0-E3), before any reaching target was even present. LFPs were recorded from 96-electrode Utah arrays implanted in the sensorimotor cortices. Spectral analyses were conducted to examine changes in alpha (8-13 Hz) and beta (14-30 Hz) band amplitudes, PAC between low-frequency (alpha, beta) phase and gamma (60-100 Hz) amplitude, and GC to assess causal interactions between cortical regions.

We found significant reward-dependent alpha and beta amplitude suppression in S1, M1, and PMd following reward cue presentation, with more substantial suppression for higher reward levels (R3 < R2 < R1). In contrast, effort-related modulation was observed primarily in PMd beta activity, suggesting a distinct role for the premotor cortex in effort representation. The combined reward-effort condition revealed a non-linear interaction where beta amplitude tracked subjective reward value, integrating effort costs.

Connectivity analyses showed that PAC was strongest in M1 for reward cues and PMd for effort cues, suggesting functionally distinct cortical networks. S1-to-M1 GC was highest in the effort-only condition, consistent with increased somatosensory processing for anticipated movement resistance. Bidirectional GC between M1 and S1 emerged in the reward-effort condition, possibly reflecting associative encoding of reward-effort cues.

These findings demonstrate that sensorimotor cortices, with distinct spatial and spectral signatures, encode expected reward and effort costs before movement initiation. Our results suggest that cortical oscillations represent movement-relevant information and contribute to pre-movement decision-making by integrating reward and effort expectations before a complete movement is planned and executed. These insights have implications for brain-machine interfaces, where contextual encoding of movement intent could enhance neural decoding strategies.

<u>1-B-17 - First in-human tests with intramuscular braided multi-electrode probes for advanced clinical electrodiagnosis and experimental use</u>

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<u>Details</u>

Over time we have developed intramuscular braided multi-electrode probes (BMEPs) for single fiber and single motor unit (SMU) myography. We are in the process of testing the feasibility of using these new probe designs for advanced clinical electrodiagnostics in humans, and experimental use in humans and animals. Variants of the probes have been tested and used in frogs and rats in our laboratory. Collected SMU data coupled with aggegate EMG and single unit neural data in frogs were recently used by us to test and exercise new algorithms to build probabilitstic models of state dependent spike effects: Stochastic Dynamic Operators (Smith, Abolfath-Beygi, Sanger and Giszter, eNeuro 2024). Efforts to translate these hardware tools to possible application in clinic has proceeded with support of Coulter-Drexel translational research grants. To explain need: there are currently three main types of commercially available clinical EMG needle electrodes (monopolar, concentric, and single fiber) which are widely used in electrodiagnostics in various clinical fields, including Neurology, Physical Medicine & Rehabilitation for motor assessments. Current clinical needle types in widespread use all have just a single channel for EMG recording. Standard of care requires anywhere upwards of 12 SMUS recorded per muscle. To obtain these requires inserting the EMG needle into target muscles multiple times and changing needle tracks in an insertion to obtain the appropriate number of single motor unit (SMU) samples for a diagnostic decision, but this repetion and probing increases discomfort and test pain level, and can reduce compliance with further tests needed. To significantly reduce multiple penetrations and provide reliable and objective test results, our strategy is to add multichannel capability to the classic EMG needle by braiding microwires onto the current clinical EMG needle designs. Multichannel probes can pick up many SMUs across distributed channels in parallel at once, and provide an opportunity to leverage simultaneous recordings and statistical features, covariations and comparisons among channels. In current first-in-human testing now approved by Drexel's IRB we will use the Natus 28G monopolar needle as the base for braiding microwires. We hypothesize this design will require no fundamental change in clinical testing practice, as it can be used with existing clinical myography systems, simply by switching among channels on an inserted needle, instead of probing for units with the needle. We have demonstrations of the features in rats and frogs needle tests, and by the time of the NCM meeting we expect to have examples of initial human recordings conducted by trained electrodiagnostic clinicians.

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<u>1-B-18 - Characterizing cortical activity during cognitive set-shifting and upper limb perturbations</u>

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<u>Details</u>

To meet the demands of an unpredictable environment, cognitive-motor interactions are necessary. The ability to switch between cognitive contexts, known as cognitive set shifting, drives changes in behavior because of a change in context. Prior work in our lab using electroencephalography (EEG) has shown that poor cognitive set shifting ability is associated with greater cortical engagement of the supplementary motor area (SMA) during a balance perturbation task¹ however, an understanding of how they are mechanistically linked remains unknown. Further, an understanding of the underlying neural mechanisms during cognitive set shifting is largely unknown due to coarse outcome metrics (i.e., time to complete (s)) and it's pen and paper nature. We will use a single device to assess cognitive set shifting performance and deliver upper limb postural perturbations to identify a common neural mechanism using EEG. The literature shows that beta oscillation activity (13-30 Hz) is reflective of maintenance of the status quo². Therefore, our primary objective is to study beta oscillations in the SMA during cognitive set shifting phases of the TMT. Our secondary objective is to associate modulation of beta activity during the TMT with SMA activity evoked by postural perturbations to the upper limb. We hypothesize that the SMA may serve as a hub for cognitive-motor interactions reflected by common neural activity in cognitive set shifting and perturbation responses that are associated with cognitivemotor function.

To test this hypothesis, we aim to collect behavioral and neurophysiological data in healthy, young adults (YA) (18-35 years) during cognitive set shifting and postural perturbations using a robotic manipulandum (KinArm End-Point Lab). For the instrumented TMT, participants will be asked to move from target to target in numerical order (TMT A) and altering numerical-alphabetical order (TMT B). Increases in time (s) between TMT B (high cognitive set shifting demand) and TMT A (no cognitive set shifting demand) will be used to define when cognitive set shifting occurs and to time lock with EEG data. To assess the underlying neural activity during cognitive set shifting, changes in SMA-related beta power recorded using EEG during cognitive set shifting epochs will be analyzed. Additionally, participants will perform an upper limb postural perturbation task in which they will resist perturbations to the hand in the forward and backward directions while standing. The magnitude of cortical evoked-responses by upper limb postural perturbations will be associated with modulation of SMA-related beta oscillations during cognitive set shifting to probe the SMA as a common mechanism.

Identifying a common neural mechanism underlying cognitive-motor interactions will bridge the mechanistic gap between cognitive set shifting and falls and help characterize how aging and neurodegenerative disorders (e.g., Parkinson's Disease) impact cognitive-motor interactions.

<u>1-B-19 - Punishing temporal judgement boosts sense of agency and modulates its underlying neural</u> <u>correlates</u>

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<u>Details</u>

When we perform voluntary actions, there is a sensation of ownership that corresponds with their execution, known as the "sense of agency", and is fundamental to the formation of action-outcome relationships. Reinforcement and its valence also change the action-outcome relationship, either through behavior promotion or diminishment. However, the relationship between reinforcement and SOA is not well understood. This study evaluated how reinforcement valence modulates SOA, via intentional binding (IB) and brain activity. 33 young healthy adults $[M_{age} \pm SD: 21.84 \pm 2.52]$ were randomly and equally allocated to one of three feedback groups [Reward (n=11), Punishment (n=11), Control (n=11)]. Participants performed counter-balanced active and passive interval estimation tasks, where either themselves (active) or the experimenter (passive) pressed a button triggering an audio tone after one of three-time intervals (200, 400, or 800ms ± 100ms random jitter) (Figure 1). Participants then estimated the length of time between the button press and tone. Estimation error (EE) was calculated as the difference in actual and estimated time and presented on a computer screen according to group assignment and accuracy. Reinforcement feedback was presented as the EE difference in different colors. An EE difference of <100ms was presented in green for Reward and white for Punishment. Conversely, EE difference of >100ms was presented in white for Reward and red for Punishment. Reward (green) and Punishment (red) were associated with monetary gain or loss respectively. Control received white EE feedback regardless of EE accuracy. IB was calculated by subtracting the mean active EE from mean passive EE, across each time interval. Electroencephalography recorded P300 amplitude from Pz, associated with EE feedback presentation. IB was lower in interval 800 compared 200 [ANOVA MD: 61.860, p=0.005] and 400 [MD: 100.172, p<0.001]. Similarly, IB was lower in interval 200 compared to 400 [ANOVA MD: 38.312, p=0.007]. Punishment increased IB between the button press and tone more than reward [ANOVA MD: 52.588, p=0.039] but not control [MD: 31.747, p=0.244]. Punishment elicited greater P300 amplitude compared to reward [RMANOVA MD: 5.554, p=0.041] and control [MD: 7.131, p=0.006]. Punishment [MD: 2.535, p=0.023] and reward [MD: 2.421, p=0.038] P300 amplitude diminished when the participants did not actively evoke the tone. Our findings showcase that reinforcement boosts SOA and modulates associated neural activity more than no reinforcement, as a function of increasing attention and arousal. These findings illuminate the effect reinforcement on behavior and brain activity by its modification of SOA, which is important for the development of treatments in neuropsychiatric diseases.

1-B-20 - Exploring motor working memory

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Details

Motor Working Memory (WM) allows the brain to temporarily store, update, and manipulate movement-related information. Yet motor WM remains largely unexplored: there is little focus on nonvisual motor information in the broader WM literature, and despite the integral role of WM in motor planning, adaptation, and long term learning, the nature of motor information held in WM is still

unclear. Here, we present a synthesis of our recent and ongoing research on motor WM, to provide new insights on this vital but understudied cognitive system.

We designed a behavioral reaching paradigm that can reliably separate limb-specific (i.e., kinesthetic) from limb-independent (i.e., abstract) content stored in motor WM. Without visual feedback, participants encode one or more reaching movements and subsequently recall movements by retracing their trajectories with the same or opposite arm. When participants recall movements with the same arm they can access the full range of information in motor WM; however, recalling with the opposite arm leaves only limb-independent information, such as spatial information, as the sole source for recall.

Using this logic and variations on the task design, we tested motor WM under different cognitive loads, time delays, and interference conditions. Notably, we found that participants did not always perform better when recalling a movement with the same arm that encoded it. Evidence from multiple experiments indicates that performing subsequent reaching movements (i.e., kinesthetic interference) degrades limb-specific representations in motor WM, yet has no effect on limb-independent representations. Unexpectedly, increasing visuospatial WM load during the motor WM task affected neither the same nor opposite arm recall, suggesting that visual and nonvisual spatial information can be stored separately in WM. To better understand how these content distinctions in motor WM may relate to motor learning, we performed a correlational study using our motor WM task and a visuomotor rotation task. We observed positive relationships between limb-specific motor WM and implicit motor learning, as well as between limb-independent motor WM and explicit motor learning. These results point to selective functional and/or anatomical parallels, and offer clues as to how motor WM supports adaptation and long term motor memory.

Taken together, our work helps bridge the gap between WM and motor cognition research. We identified dissociable, limb-specific, and limb-independent components within motor WM, which challenges traditional WM models that either overlook or subsume motor information into visuospatial WM. Furthermore, the selective relationship between these distinct WM components and implicit and explicit motor learning suggests the need to revisit and fully integrate motor WM into models of cognitive motor processes.

<u>1-B-21 - Sensitive 3D whole-face movement detection and and synchronized electrophysiological</u> <u>analysis in mice</u>

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<u>Details</u>

Synchronous movements, large and small, of the entire face, from grimacing to chewing, offer significant insights into internal states. Mice, with discernible facial responses and evolutionarily conserved mammalian facial movement control circuits, provide an ideal model to unravel the link between facial movement and internal physiological states in mammals. While complex facial movements are orchestrated synchronous activity of muscles spread throughout the face, existing

frameworks lack the spatial or temporal resolution to sensitively track subtle motion of the entire mouse face, due to its small and conical form factor. We introduce Cheese3D, a computer vision system that uses a calibrated six-camera array to capture high-speed motion of the entire mouse face (including ears, eyes, nose, whisker pad, mouth, while covering both sides of the face). Adapting components from existing markerless pose estimation tools, we carefully designed a hardware and software pipeline to create a unified 3D view of the mouse face, and introduced technical advancements to reduce keypoint jitters common to existing tools, hence increasing resolution and sensitivity necessary to confidently detect subtle and rapid mouse facial movements. By tracking motion in 3D, our interpretable framework extracts dynamics of anatomically meaningful facial features in absolute world units at sub-millimeter precision. Recent improvements to Cheese3D combine rich behavioral dynamics with a combination of temporally synchronized neural recordings, including in vivo electrophysiology of brainstem motor network, high-density electromyography (EMG) of rodent facial musculature, and electroencephalography (EEG). The functional analyses allow Cheese3D to provide clear physiological insights, as shown by proof-of-principle experiments across behaviors, including inferring muscle and jaw anatomy from fast chewing motions, accurately predicting depth of general anesthesia using facewide changes, and functional mapping facial motor nucleus by linking subtle facial motion to patterned electrical stimulation and recording. Cheese3D can serve as a discovery tool that renders facial movements highly interpretable as a readout of otherwise hidden internal states.

1-B-22 - Neural representation of internal models for sensorimotor planning

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Details

Internal models of the sensory environment enable efficient motor planning by simulating the sensory consequences of movements. However, it is not well understood how these models are represented neurally, independent from lower-level features of movement. Here, we developed an fMRI reaching task where participants made the same movements to reach the same sensory goal (target), but under differently structured sensory perturbations (visuomotor rotation versus mirror reflection). This required the participants to plan their movements using distinct internal models, despite the lower-level features (e.g. target location and optimal reach angle) being identical.

In this task, participants moved a joystick to control a cursor to make a center-out reach toward one of four possible targets on the screen, for 18 blocks. Before each block, participants were informed about what perturbation they will experience (visuomotor rotation, where the cursor rotated clockwise away from the hand, or mirror reversal, where the cursor reflected off a vertical mirror axis). Critically, for two of the four possible goal locations, the optimal hand reach angle and endpoint visual feedback were identical under both rotation or reflection perturbations. Before executing each reach, participants saw the target location for a jittered interval (2-4s) and were instructed not to move (planning phase). Participants were given only 1 second to make their movements, which meant that they had to make a movement plan before execution, during the planning phase. After movement execution, visual feedback on the accuracy of the reach was delayed by 1 second after completion to isolate explicit learning processes and limit the contribution of implicit sensorimotor recalibration.

We used the BOLD data from the planning period of the trials where the lower-level features of movement plans should be identical to classify which internal model (rotation vs. reflection) participants were employing. Specifically, we trained classifiers on searchlights across the whole brain to explore

where these distinct models are represented. Preliminary results suggest that areas such as the right superior frontal gyrus (implicated in inhibition during task switching, e.g. Aron et al., 2004), bilateral superior parietal lobe (involved in sensorimotor integration, e.g. Wolpert et al., 1998), and the bilateral occipital lobe (associated with motor imagery for planning, e.g. Hanakawa et al., 2008) represented abstract internal models for planning. Ongoing analyses, including representational similarity analysis of neural activation patterns, will also help clarify the specific task information represented in these regions.

1-B-23 - Similar patterns of online target selection with the dominant and non-dominant arm

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<u>Details</u>

Most people prefer using the right arm for movement tasks whether specialized or generic, e.g. overhand throwing versus reaching to a static target. This consistent preference likely reflects differences in the relative capabilities (and underlying circuits) of the dominant and non-dominant arm as shown in various paradigms of unperturbed movements and compensation to visuo-motor rotations and perturbing loads. It remains unexplored how the two arms compare in tasks that require rapid online decisions, a behavior required in a world with time-varying options. We previously reported that participants who are forced to re-direct their forward moving hand to either a left or right target will make faster and more accurate decisions when instructed to select the option that is "near" the original goal than when instructed to select the option "far" from the original goal. And in both cases, the online reaction time was delayed compared to redirecting the arm to a single target which jumped left or right mid-reach. Here, we ask whether this pattern of online decision-making differs between the dominant and non-dominant arm. Superior performance by the dominant arm would implicate those neural networks for fast action selection. 21 right-handed participants (11F, 10M, mean age = 24.1) performed with a robotic device exoskeleton and a coupled projector system (Kinarm Exo, BKin Technologies). The task involved reaching forward to a default target 20 cm ahead of the starting target and occasionally redirecting to lateral target jumps (+/- 2 or 5 cm) or the instructed near or far option during target splits (+2&-5 cm and -2&+5 cm). The online reaction time (oRT) of the right arm to a target jump was ~165 ms compared to ~170 ms by the left arm ($F_{1,20} = 4.26$, p = 0.052). With target splits, participants had faster oRTs with the "Near" instruction (~230 ms) compared to the "Far" instruction (~250 ms), ($F_{1,20}$ = 9.54, p = 0.006) but inter-arm differences were smaller and not statistical different (\sim D10 ms, F_{1,20} = 9.54, p = 0.1). The same patterns occurred with accuracy of online target selection; significantly differences between instruction ("Near" ~80% vs "Far" ~68%, $F_{1,20}$ = 17.13, p < 0.001) but not between arms $F_{1,20}$ = 1.77, p = 0.2. The within-arm patterns in this present study align with our previous report. The differences between the dominant and non-dominant arm were small and variable (usually not significant) suggesting that arm preference depends on factors other than processes for online decisionmaking.

1-B-24 - Auditory input regulates vocal tract constriction dynamics during speech production

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<u>Details</u>

A central issue in the study of speech motor control is determining how the nervous system uses auditory input to coordinate and control articulator movements, whose function is to produce speech sounds by forming constrictions in the vocal tract. However, the role of auditory input in the control of articulator movements has, for the most part, only been studied using indirect acoustic measures. Here we directly examined coordination of tongue-tip and jaw kinematics (position and velocity) during the production of stop consonants in 16 unique vowel-consonant-vowel (VCV) utterances when audition was masked. Nine subjects with normal hearing produced the target VCV utterances, recorded using state-of-the-art electromagnetic articulography, with variation in production rate (fast-normal) and syllable stress (first syllable stressed-unstressed). V was $/\alpha/-\epsilon$ and C was /t/-/d/. Utterances were split between two listening conditions: unmasked and masked (16 utterances x 15 repetitions x 2 listening conditions = 480 kinematic and acoustic recordings/subject). To quantify the effect of auditory input on the coordination between the tongue-tip and jaw, the timing relations between peak velocities were determined during constriction formation for intervocalic C. Across both listening conditions, the timing of articulator peak velocities was tightly coupled across scalar changes in rate and stress, such that timing variation in one articulator was accompanied by proportional changes in the timing of the other articulator. Thus, the timing of peak velocities for the tongue-tip and jaw appear to be adjusted as a group rather than individually in service to speech production. Furthermore, the timing of peak velocities for both articulators were reliably differentiated based on the rate/stress pattern of the utterances. During auditory masking, however, tongue-tip latencies, but not jaw latencies, were found to be less reliably differentiated by each rate/stress pattern. These findings suggest that, during speech production, the nervous system relies more heavily on auditory input to control the timing precision of tongue-tip movements than jaw movements. Two alternative, but not mutually exclusive, explanations are considered: (1) The optimal execution of movements involving the tongue-tip rely more heavily on auditory input than those involving the jaw because tongue-tip movements are subtler and require greater dexterity of control (i.e., more independent muscular degrees of freedom). (2) The nervous system is better able to adapt and utilize somatosensory inputs from the vocal tract to control jaw movements than tongue-tip movements when the auditory system is temporarily incapacitated.

Highlights of submission:

- 1. Timing is the basis of control for inter-articulator speech coordination.
- 2. Auditory input regulates the precision of timing during constriction formation for speech sounds.
- 3. Auditory masking induces aberrant tongue kinematics during inter-articulator speech production.

Justification statement:

A core question in the domain of communication neuroscience, is how the nervous system uses auditory input to coordinate and control vocal tract movements in service to speech production. This question has important bearings on the sensory feedback control of movement, yet its answer remains unclear because speech production has for the most part only been studied using indirect acoustic measures. In this study, we used electromagnetic articulography to capture direct kinematic measures (position and

velocity) of jaw and tongue-tip movements during the production of speech, with and without auditory masking.

<u>1-B-25 - Modulation of the activity of neurons in the primary motor cortex (M1) by the premotor areas</u> and the posterior parietal cortex

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<u>Details</u>

Introduction: The refinement of hand movements and the increased complexity of motor behaviors in primates are associated with the establishment of more direct connections of M1 neurons onto cervical motoneurons controlling the hand and the appearance of additional premotor and sensory areas. We recently conducted a series of experiments using paired-pulse stimulations and electromyographic recordings in capuchins, a species capable of dexterous finger movements and complex motor behaviors such as tool use. The goal was to compare the pattern of modulations of the dorsal and ventral premotor cortex (PMd and PMv) and the supplementary motor area (SMA) with M1. We used pairedpulse stimulation protocols with a broad range of interstimulus intervals. We found that each premotor area has a unique pattern of facilitation and inhibition across ISIs, which could allow them to modulate M1 neurons in different ways. One limitation of these experiments is that they provide limited information about where in the central nervous system the distant cortical area modulates the outputs of M1. Therefore, the main objective of the current study was to determine how different cortical areas within the same hemisphere modulate the activity of M1 neurons. Methods: In capuchin monkeys, chronic electrode arrays were implanted in the hand representation of M1 (recording site) and in PMv, PMd, and Area 5 (conditioning sites) within the same hemisphere. In each recording session, a few stimulation electrodes from each conditioning area were selected to deliver single-pulse stimulations (0.2 ms cathodal pulses) at 4 Hz while recording in M1. Stimulations were randomly delivered until a total of 1000 trials were accumulated from each of the stimulation electrodes. Results: A total of 260 M1 neurons were recorded, with modulation observed in 76%, 81%, and 77% of neurons following stimulation in PMd, PMv, and Area 5, respectively. A variety of modulatory responses were observed. A significant number of neurons showed an exclusive increase in their firing (pure facilitation) across conditioning electrodes in a given area (18.8% of M1 neurons for PMd stimulation, 16.9% for PMv, and 16.5% for Area 5). Pure inhibition and mixed responses were present at lower frequencies. Analyzing the latencies of the modulatory events revealed that PMd exhibited early peaks of modulatory inhibition (around 8 ms), whereas PMv and Area 5, in addition to the early modulations, showed more prolonged and delayed responses lasting up to 93 ms post-stimulation. In addition, analysis of the incidence and magnitude of significant modulation indicated that PMv tended to evoke the most robust facilitation effects compared to the other areas. Conclusion: Data from this project shed light on how information from various cortical areas is integrated in a distinct way within the neuronal population in M1 and highlight potential differences between the contributions of different premotor and parietal areas.

1-B-26 - ATHENA: automatically tracking hands expertly with no annotations

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<u>Details</u>

The human hand allows for dexterous manipulation unparalleled by any other living organism. As a result, humans can perform a rich repertoire of tasks using their hands, ranging from activities involving delicate finger control to forceful grasps. Conventionally, hand movements are recorded through expensive marker-based optoelectronic cameras that are prone to occlusion or time-consuming manual annotations of video recordings. The limitations of these systems have compelled researchers to predominantly study hand behaviours during simple movements within constrained in-lab settings that fail to capture the rich breadth of hand capabilities. To understand neural control of the hand, we need to study naturalistic hand behaviours that reflect how individuals learn complex skills in real-world settings. As such, the purpose of our work was to develop and share an open-source Python-based toolbox for performing three-dimensional markerless tracking of the hands. Our toolbox uses Google's MediaPipe Solutions to automatically identify 2D locations of 42 key points bimanually across the hands and 33 key points across the entire body. The 2D key point locations from each camera view are triangulated to 3D. The 3D locations are then refined using a multi-step procedure that improves the identification of left and right hands, and iteratively smoothes the data in combination with a biomechanical constraint enforcing segment lengths to remain close to the median lengths of each segment. The toolbox supports parallel processing of cameras and runs offline at approximately 0.25x real time for an 8 camera setup. The toolbox, ATHENA, is available on GitHub and requires minimal dependencies (e.g., GPU is optional and no machine learning libraries are required). Upon installation, users will be presented with a simple graphical user interface where users are prompted to select video recordings and associated camera calibration parameters, and optionally can adjust any analysis options (e.g., tracking confidence, filter cut-offs) for easy processing of kinematic data. To validate the toolbox, we are currently comparing the accuracy of the hand kinematic measurements (e.g., grip aperture, finger joint angles) from the markerless system against an optoelectronic marker-based system (OptiTrack) during controlled unimanual reach-and-grasp movements as well as bimanual hand-object manipulation as representative of activities of daily living. In doing so, ATHENA will allow users to quantify hand kinematics during gross free-hand movements and fine precision tasks involving object interactions with both hands while exhibiting comparable tracking performance as marker-based technologies. Overall, we aim to share an easy-to-use, accurate solution for 3D tracking of the hands to facilitate future motor control and learning studies for investigating naturalistic hand behaviours.

<u>1-B-27 - Evaluating grasp-related tuning differences in the macaque frontoparietal grasping network</u>

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<u>Details</u>

In everyday life, primates display a variety of grasping movements that are influenced by object characteristics such as fragility, surface size, texture, and weight. As a result, specific grip types are used depending on the particular object and the intended action.

The frontoparietal grasping network, the anterior intraparietal area (AIP) and ventral premotor cortex (F5) play a key roles in planning and executing grasping movements. Many studies have examined visuomotor transformations within and between these areas. However, due to methodological constraints, little is known about how neural population dynamics are distributed within them.

To investigate intra-areal differences in neural activity, we trained a female *Macaca mulatta* to perform a visually instructed delayed grasping task. Using Neuropixels probes, we recorded from 384 channels per day at different locations in AIP and F5. Spike sorting was performed with Kilosort4, but due to its limitations in handling fast neuronal drifts, we used the Dredge package for superior drift correction.

We examined whether a visuomotor gradient exists across different recording sites in AIP and F5. To compare responses, we computed the variance of neuronal populations across conditions to assess condition-dependent modulation strength.

In both AIP and F5, the movement epoch captured the most variance while visual and preparatory epochs explained similar level of variance, though the latter was higher in F5 than AIP. In AIP, modulation strength increased linearly across epochs at anterior sites. However, at more posterior and more medial sites, movement-related modulation strength decreased, while visual and preparatory-related modulation strength increased. In F5, a U-shaped gradient emerged. The second most lateral site captured the most modulation strength during the movement epoch, while the most medial site showed the highest modulation strength during the visual and preparatory epochs. These results suggest that the lateral part of the area is more movement-related, while the medial part is more preparatory and sensory-related.

To further explore the presence of a gradient, we applied marginalization to the session, location, and neuron factors. The greater variance explained by the location factor, compared to the session factor, supports the idea that we recorded distinct neural populations at the same site with shared population properties.

Our findings suggest, contrary to previous studies, that a simple linear gradient does not consistently apply to either area. Instead, it may be more accurate to divide these regions into subareas to better characterize grasp-related differences.

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1-B-28 - Sequence preparation is not always associated with a reaction time cost

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Details

In daily life, individuals perform sequences of movements that require speed and accuracy. Previous work reveals that when participants are presented with more sequence elements, their reaction time (RT) increases. This RT cost has been taken as evidence that preparation of multiple movements is taking place before initiating the first movement. Here, in the context of sequential reaching movements, we show that participants do prepare multiple movements without incurring any RT cost. Instead, the RT cost solely reflects the ambiguity of the first movement target.

Participants performed a reaching task with targets from a hexagonal grid with 4 cm spacing. Targets were chosen so each new target was in one of the neighboring positions relative to the current target. We independently manipulated three factors. First, we manipulated the number of targets shown to the participant (Horizon), either one or two (H1, H2), to assess whether participants could prepare beyond the first movement. In the H2 condition, the order of the targets was indicated by their brightness. Secondly, we instructed participants to perform either a single reach or a sequence of two reaches. By keeping visual stimuli constant and manipulating reach count, we dissociated sequence preparation effects from first-target ambiguity. Finally, we manipulated the spatial arrangement of targets in the H2 condition. In the non-spatial condition, both targets were equidistant from the home position, forcing participants to rely on brightness cues to identify the first target. In the spatial condition, the two targets were positioned at different distances from the home position, allowing participants to use both distance and brightness cues to identify the first target. This manipulation allowed us to vary the number of choices for the first target independently of the number of targets displayed.

To verify that participants really took the second target into account before initiating the first movement, we showed that the second target could be predicted from the first reach kinematics early from movement onset. This effect was absent when only a single reach was performed in the H2 condition, indicating that there is a motor plan for the second target only when two reaches are intended. Regarding RT, we observed no RT cost when participants performed two reaches compared to a single reach, indicating that there is no RT cost due to sequence preparation. We only observed RT cost across horizons in non-spatial trials in which participants had to use brightness to identify the first movement target. This RT cost was completely eliminated in spatial trials, suggesting that spatial ordering facilitates identifying the first target.

Our study demonstrates that the RT cost observed when initiating longer sequences is solely associated with the ambiguity of identifying the first movement target and that multiple movements are prepared before the first movement initiation without any RT cost.

1-B-29 - Pragmatic representations of self and other's action in the monkey putamen

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<u>Details</u>

The primate putamen nucleus receives convergent projections from parietal and frontal areas encoding both executed and observed actions. Yet, whether and how putamen neurons encode self and others' actions remains unknown. Here, we recorded single-neuron activity from an anatomically characterized region of the putamen in macaques performing a Mutual Action Task (MAT) with a human partner. During the MAT, the partners took turns to perform or observe the partner grasping the same multiaffordance object. We found neurons discharging selectively during the monkey's own action, the experimenter's action, or both. The grip type was encoded during self, but not partner's, trials. Viewing the partner's action was neither necessary nor sufficient, as neurons discharged even when the partner's action occurred in the dark, but not if it was viewed through a transparent barrier. Our findings support a pragmatic role for putamen neurons in gating action execution while observing others in social contexts

<u>1-B-30 - Differential representation of initiation and execution of locomotion in cortical and striatal</u> <u>circuits</u>

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<u>Details</u>

Multiple brain areas, including cortex and basal ganglia, are believed to contribute to the initiation and execution of locomotion. Previous work has identified neurons in primary motor cortex (M1) that fire phasically during the step cycle of locomotion. Additionally, movement initiation related activity has long been observed in prefrontal cortex (PFC) and striatum. However, a comprehensive comparative analysis of the extent to which motor coding is represented in different brain regions is lacking. Here, we compared the neural encoding of the initiation and execution of walking across M1, dorsolateral striatum (DLS), dorsomedial striatum (DMS), and PFC, during self-initiated locomotion in mice. We performed high-speed video recordings of unrestrained locomotion of mice walking in an open field and monitored limb positions using animal pose tracking tools. Simultaneously, single-unit spiking activity was recorded using 64-channel silicon probes. We first found that during walking, the majority of units in M1 and DLS are phase locked to the gait cycle of individual limbs. By contrast, gait phase-locked neurons were significantly sparser in PFC and DMS. We then decoded single-limb gait phase using population activity. We pooled data across multiple mice and sessions to increase the number of neurons for decoding. While gait phase could be decoded from all four recorded brain structures, the decoding accuracy was significantly higher when using an ensemble of M1 neurons compared to other regions. These findings suggest that M1 more reliably represents rapid step-by-step changes in movement at the population level. Next, to evaluate whether these areas represent the start of movement, we decoded the time to movement initiation from population activity. We found that M1, DLS and DMS but not PFC showed comparable decoding accuracies at movement onset. Taken together, these results demonstrate that the initiation and execution of locomotion are differentially represented across cortical and striatal circuits, with M1 containing an enriched population code for single-limb gait.

<u>1-B-31 - How plan-based generalization affects the apparent relationship between explicit strategies</u> and implicit recalibration

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Details

Motor adaptation is supported by at least two primary processes: explicit strategies, which involves conscious and deliberate changes in motor planning, and implicit recalibration, which operates unconsciously and automatically. The degree to which these two processes interact during sensorimotor adaptation and their downstream consequences on implicit learning remains an open question. While early work assumed that these two processes combine linearly to produce overall learning, more recent work has challenged this view. However, these studies may have underappreciated complex spatial and temporal dynamics that could indirectly affect the apparent interaction between explicit aiming and implicit recalibration. In particular, implicit recalibration exhibits plan-based generalization, where its peak is centered on explicit movement plans rather than target locations. As a result, shifts in an explicit strategy will systematically alter the spatial expression of implicit recalibration. Likewise, implicit recalibration appears to unfold over multiple time scales, with stable and volatile components whose relative contributions vary based on measurement timing and experimental design choices. Without independent measurements of both processes and clear task comprehension of the participants, an invalid conclusion about their relationship could be reached. To determine whether these confounding factors could mask additivity tests between explicit strategies and implicit recalibration processes, we conducted a within-subject visuomotor rotation task, obtaining independent measures of both processes using both aim-report and Process Dissociation Procedure (PDP) while also taking into account potential effects of spatial and temporal dynamics. We find a strong inverse relationship

between explicit strategies and implicit recalibration processes after accounting for task comprehension and plan-based generalization with minimal impact from temporal dynamics. However, the relationship between these processes was subadditive, suggesting that there is either a fundamental nonlinear interaction between these processes or a persistent limitation in current experimental methodologies designed to suss out their operation.

1-B-32 - The role of sensory consequences in movement replication

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Details

Learning a motor skill requires adjusting unsuccessful movements and repeating successful movements. How to repeat a successful movement? Models of reward-based motor learning formalize this as repeating the motor command that resulted in the successful movement, with no role for the sensory consequences of the movement. Here, we ask whether humans replicate a successful movement by repeating the motor command or by repeating its sensory consequences.

We asked 32 healthy participants to join a reward-based elbow flexion experiment without visual feedback of the arm. They first performed flexion movements to visual targets (baseline). During half of the trials, the antagonist triceps muscle was vibrated with a frequency of 120 Hz from movement onset to offset. Antagonist muscle vibration induces an illusory muscle lengthening and a corresponding undershoot of target-directed movements. This way, the actual sensory consequences differ from (i.e. undershoot) the predicted sensory consequences from the motor command.

Participants then performed elbow flexion movements of self-chosen amplitudes to hit invisible targets. After each movement, success-failure feedback signaled whether a target was hit or not. Upon success, participants replicated this successful movement as precisely as possible. On half of the successful trials, the triceps muscle was vibrated to change the sensory consequences of the motor command (i.e. undershoot). We focus on movement replications without vibration to distinguish two hypotheses: If participants repeated successful sensory consequences, they would match the flexion angle of the successful movement. Conversely, if participants repeated successful motor commands, they would overshoot relative to the successful movement. We first took the average angular change between successful trials with vibration and their subsequent replication without vibration, and we then divided this by the vibration undershoot that was obtained during the baseline (visual targets). The resulting replication fraction indicates to what extent participants repeated sensory consequences (zero) or motor command (one).

Participants showed a vibration-induced undershooting, both when moving to baseline visual targets (mean 3.7°, \pm 1.8° SD) and when repeating non-vibrated successful movements (1.4° \pm 2.0°), a hallmark of muscle vibration. Participants varied their movement amplitudes more following failed (16.3° \pm 4.2°) than following successful (3.6° \pm 0.9°) movements, a hallmark of reward-based motor adjustments. Crucially, participants showed a mean replication fraction of 0.4, \pm 2.0 SD.

We found no evidence for the hypothesis that participants repeat a successful motor command. We conclude that when replicating a successful movement, participants do take into account the sensory consequences at the end of that successful movement. This is at odds with the way current models of reward-based motor learning formalize movement replication.

1-B-33 - Handwriting movements are pre-ordered individually prior to sequence execution

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Details

Monkey neurophysiology findings have shown that elements of a drawing sequence are planned in parallel before execution, a process known as competitive queuing (CQ). This finding has been replicated in humans through MEG and behavioural studies focused on typing sequences. However, it is still unclear whether the preplanning of individual movements persists in more continuous skilled actions that involve greater biomechanical complexity. To test this, we investigated how movement kinematics impact sequence planning in a handwriting-like task. Specifically, we asked whether the fusion of velocity curves between adjacent movements affect movement preparation. Participants trained for two days to perform two sequences of four sequential centre-out-and-back movements. To manipulate fusion, participants performed sequences from memory after a Go cue in one of three conditions: acute, right-angle, and obtuse angles between sequential targets. Probe trials consisting of single movements measured planning by assessing movement availability at each sequence position.

All groups showed a decrease in movement time (p<.001) and initiation time (p<.001) from the first block of training to the final test block. Participants did not achieve full fusion during the task, consistent with naturalistic handwriting, where movements are only partially fused. There was an interaction effect between group and block for fusion (F(2,55)=5.06,p=.01, η 2=.023), with the right-angle (p<.001) and obtuse groups (p<.001) showing a significant increase in fusion, as these angles reduced kinematic jerk.

Results showed a significant effect of sequence position on both RT (F(3,165) = 43.8, p < .001, $\eta^2 p$ = .065) and error rate (F(2.54,139.83) = 4.81, p = .005, $\eta^2 p$ = .042), indicating that movement strokes associated with later sequence positions were less accessible, leading to slower and less accurate execution. These position-related differences suggest that competitive queuing (CQ) occurred across groups. Furthermore, a significant interaction between group and position was found for both RT (F(6,165) = 2.78, p = .013, $\eta^2 p$ = .009) and error rate (F(5.08,139.83) = 8.01, p < .001, $\eta^2 p$ = .13) with the obtuse group demonstrating a more pronounced CQ gradient, contradicting the fusion hypothesis.

Importantly, the strength of movement pre-ordering during planning was not associated with kinematic fusion during execution, as fusion was not correlated with CQ (RT: rho=-.058, p=.67; error rate: rho=.15, p=.25). In contrast, but consistent with previous findings in finger press sequences, we found that a more pronounced CQ gradient was associated with faster initiation of correct sequences (RT: rho = -0.3, p = .022). Our results indicate that stronger kinematic fusion does not result in the formation of new movement primitives that are planned as one movement but instead continue to be prepared separately.

1-B-34 - Hierarchical neural dynamics in motor cortex and striatum across naturalistic behaviors

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<u>Details</u>

Naturalistic behaviors involve many movement components, from precise targeted reaches to innate motor sequences such as grooming. One challenge the nervous system faces is the need to accurately carry out each of these movements while also being able to flexibly switch between them. Motor cortex

and striatum have previously been implicated in the execution and selection of motor actions, but how their activity dynamics are organized across naturalistic movement is still poorly understood. Previous studies have focused on interrogating the function of these regions using either highly constrained, individual movements, or sampling a narrowly circumscribed set of movements in a simplistic open field paradigm. Whether these regions engage specific subpopulations or specific modes of coordinated activity across a wide range of behaviors, and how these activity patterns are related to muscle activity throughout the full behavioral space is unknown. To address this, we developed a novel paradigm that allows for the investigation of neural dynamics across behaviors that require agility and dexterity, such as climbing and walking across an irregular grid, and innate behaviors such as eating and grooming. We used UMAP projections of muscle activity to parcellate the behavioral space into distinct states. In order to interrogate the organization of neural dynamics across these behavioral states, we chronically implanted neuropixels probes to simultaneously record hundreds of neurons in the caudal forelimb area of the motor cortex and the striatum. We identified striatal and cortical neurons whose activity ranged from highly selective for individual behaviors to uniform across all behaviors, and found greater behavioral specificity within striatum compared to cortex on an individual neuron level. Conversely, using canonical correlation analysis, neural decoding, and EMG triggered averaging, we found greater encoding of muscle activity within cortex compared to striatum across all behaviors. On a population level, we discovered both distinct neural subspaces corresponding to separate sets of behaviors as well as highly overlapping subspaces among more similar behaviors in both regions. We propose a model whereby striatal neurons encoding action state inform separate pattern generating circuits, including the motor cortex, to transition between different dynamical regimes throughout naturalistic behavior.

1-B-35 - Neural dynamics switch between motor preparation and execution

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<u>Details</u>

The control of movement sequences relies on a dynamic interplay between movement planning and execution. Invasive recording in non-human primates show that preparatory and execution activity patterns are distinct and orthogonal to each other when projected into lower-dimensional spaces, with neural dynamics "rotating" from the preparatory to the execution subspace. Despite robust evidence from animals, this dynamic transition remains less well understood in humans. While fMRI studies have confirmed neural pattern shifts in humans, the precise temporal dynamics and the role of regions beyond the motor cortex remain unclear.

In this study, we employed multivariate pattern analysis and dimensionality reduction techniques to disentangle the temporal dynamics of preparatory and execution-related neural signals recorded using magnetoencephalography (MEG) across the head and in primarily motor and supplementary motor cortices using source reconstruction. Participants performed a delayed sequence production task in a jittered delay paradigm, isolating neural activity associated with planning and execution phases.

Our findings reveal that Our MEG signals during preparation and execution occupy distinct subspaces, as demonstrated through principal component analysis (PCA) for dimensionality reduction. A Linear Discriminant Analysis (LDA) pattern classifier successfully decoded finger sequences from both preparatory and execution states for but showed non-overlapping prediction curve between the sequence patterns related to the two states. By aligning the classifier output to different phases, results indicate that the state transition begins 268ms (sd = 69ms, p <0.01, N = 15) after the Go cue and

completes 420ms (sd = 149ms, p<0.01, N = 15) before movement initiation, jittered according to the target initiation time. Further investigation using source localization revealed distinct dynamic patterns in the primary motor and supplementary motor areas, providing a clearer representation of the dynamic switch between baseline, preparatory and execution states within these areas (98% variance explained). Using unsupervised Gaussian Mixture Models on source-reconstructed data, the model classifies the neural state at each time point. It achieves an average prediction accuracy of 73.6% for the preparation state and 72% for the execution state in the motor cortex, and 79.6% for preparation and 85.8% for execution in the supplementary motor area.

These findings show that non-invasive recordings can reliably capture the transition between action preparation and execution across the brain and in individual regions of interest. By distinguishing preparatory from execution-related neural dynamics, this work advances the interpretation of non-invasive motor recordings and lays the foundation for improved neural decoding in movement research.

C – Posture and Gait

1-C-36 - Neural correlates of walking and reaching in the monkey lateral frontal cortex

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<u>Details</u>

Monkeys rely on specialized cortical circuits for precise motor actions, such as reaching and grasping, which are distinct from the spinal cord's central pattern generators responsible for automatic movements like quadrupedal walking. However, unlike the stereotyped walking seen on a treadmill, natural walking often requires precise limb placement, speed adjustments, and directional changes, which depend on cortical involvement. In this study, we examined the role of the lateral frontal cortex, a region primarily associated with voluntary arm movements, during natural, spontaneous walking. We recorded single neuron activity from the lateral frontal cortex of two macaques while they were freely walking and reaching for food within a large plexiglass enclosure. Among 470 neurons recorded across 11 sessions, 79 (17%) showed phase-specific activity during the walking cycle, often peaking during the contralateral forelimb's extension phase just before surface contact. Neural responses varied across steps, with several walking-related neurons differently modulated based on whether the step was taken on flat ground or an elevated wooden structure. Additionally, one third responded preferentially to the first, last, or intermediate steps of a walking sequence. Comparing responses during walking and reaching-grasping revealed that over half of the neurons active during walking also responded during the reaching phase of grasping actions. Electrical microstimulation of sites hosting these walking-andreaching neurons confirmed their causal involvement in forelimb or axio-proximal movements. Together, these findings indicate the presence of walking-related activity in the lateral frontal cortex and support the long-standing hypothesis on the existence of a shared neuronal substrate for reaching and voluntary locomotor control.

1-C-37 - Human-human physical interaction in a challenging postural balance task

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<u>Details</u>

Maintaining postural balance requires complex neuromuscular control that can be affected by aging and neuromechanical impairments. Understanding neural control of postural balance is also key to predict and prevent falls. Previous studies already established that touching a stable surface, even with a small contact force, reduced postural sway. Yet, the benefits of holding the hand of another individual providing unstable but interactive support remain largely unexplored.

This study examined the effect of 'holding hands' on postural balance between two partners with different skill levels. To simulate unstable balance as in impaired populations, subjects stood on a narrow beam. We hypothesized that pairing with a same-skilled partner enhances balance, while an expert paired with a not-trained partner experiences performance degradation.

Participants stood in a tandem stance on a narrow beam (width 3.65cm, height 7.62cm). Experts (n=14, ballet dancers) executed the task coupled with a novice and an expert, while novices (undergraduates, n=10) were coupled with a novice partner. Both groups were also tested standing alone. During the coupled conditions, partners stood side by side on a narrow beam, placed on a force plate, both facing forward, holding the same handle of a compliant robot. Each coupling condition was performed in 10 consecutive trials (30s each). We recorded the kinematics of the focal participant's body motion to calculate the center of mass (CoM), ground reaction forces to obtain the center of pressure (CoP), and the robotic handle force. Dependent measures were the velocity of the CoM and the CoP. As participants frequently stepped off from the beam, the step-offs were also a metric for evaluating the goodness of the performance.

In the single conditions, novices stepped off the beam more frequently than experts and exhibited greater CoM velocity and CoP fluctuations, as expected. Yet, when 'holding hands' with a novice partner, all dependent measures decreased, reaching expert values. Counter expectations, all experts' metrics remained unaffected by physical coupling, indicating that experts were neither perturbed by a non-trained partner, nor stabilized by a skilled partner. The haptic forces exchanged between partners via the robotic handle are under investigation.

By showing that novices improved when coupled with another novice, our study highlights the ability of the CNS to exploit haptic information. The fact that experts maintained their performance, even with a less skilled subject, indicated that they were able to reject perturbations. These findings underscore the important role of haptic sensation in postural balancing and highlights the need to further investigate the bi-directional haptic communication. Insights into partner support have the potential to inform rehabilitation strategies and the design of assistive devices.

<u>1-C-38 - Computational modeling of sensorimotor circuits and interactions controlling cycle and phase</u> <u>durations during locomotion following spinal cord injury</u>

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<u>Details</u>

Locomotion is controlled by spinal circuits that interact with supraspinal drives and sensory feedback from the limbs. These sensorimotor interactions are disrupted following spinal cord injury. To investigate the effects of an incomplete spinal cord injury (right lateral thoracic hemisection), on the operation of the spinal locomotor network, we used a computational model of cat locomotion we recently published (Rybak et al., 2024) to investigate and predict post-injury changes in cycle and phase durations during treadmill locomotion in tied-belt (equal left-right speeds) and split-belt (unequal leftright speeds) conditions. Based on our model, we hypothesized that following hemisection the contralesional ('intact', left) side of the spinal network is mostly controlled by supraspinal drives, whereas the ipsilesional ('hemisected', right) side is mostly controlled by somatosensory feedback. We then compared the simulated results with those obtained during experiments in adult cats before and after a mid-thoracic lateral hemisection on the right side in the same locomotor conditions. Our experimental results confirmed many effects of hemisection on cat locomotion predicted by our simulations. We show that having the ipsilesional hindlimb step on the slow belt, but not the fast belt, during split-belt locomotion substantially reduced the effects of lateral hemisection. The model provides explanations for changes in temporal characteristics of hindlimb locomotion following hemisection based on altered interactions between spinal circuits, supraspinal drives, and somatosensory feedback.

Rybak IA, Shevtsova NA, Markin SN, Prilutsky BI and Frigon A (2024). Operation regimes of spinal circuits controlling locomotion and role of supraspinal drives and sensory feedback. eLife. 13:RP98841.

<u>1-C-39 - Vestibulospinal neurons respond to support surface perturbations in a freely-behaving rhesus</u> <u>macaque model of postural control</u>

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Details

Generating appropriate postural responses to maintain stability in a dynamic environment requires distinguishing unexpected self-motion arising from external perturbations, from intended self-motion arising from active behavior. Previous studies aimed at understanding the neural control of posture have largely relied on behavioral and EMG studies, which, while informative, are limited by noninvasive methods and comparisons between healthy subjects and those with sensory or motor pathologies. Different phases of postural responses are thought to emerge from distinct sensory modalities—somatosensory, vestibular, and visual—and involve interactions between reflexive mechanisms and voluntary behavior. However, distinguishing the contribution of each sensory modality to the different temporal phases of the postural response necessitates simultaneous recording of neural activity and behavior.

Neurons in early vestibular pathways, which drive reflexive postural responses, respond robustly to unexpected self-motion but exhibit reafference suppression. This results in a marked attenuation of their response to actively-generated motion, despite the context-invariant encoding of head motion by vestibular afferents. We hypothesize that initial head motion elicited by external perturbations is encoded by vestibulospinal pathways to drive postural responses. However, once the initial reflexive response is triggered, the overall head motion results from a combination of the perturbation, the

reflexive response, and voluntary behavior. Consequently, neuronal responses to head motion will be attenuated.

To test this hypothesis, we first developed a rhesus monkey model of postural control. Specifically, we recorded behavioral responses to transient tilts. Monkeys were trained to adopt a standard posture on a force plate mounted to a hexapod motion platform while wearing a head-mounted IMU. Control animals were able to compensate for the unexpected motion, resulting in very small head and body movements. In contrast, monkeys with bilateral vestibular loss showed maladaptive responses that were hypermetric and in the reverse direction of normal. Notably, this maladaptive response exhibited a shorter latency than normal, providing behavioral evidence that vestibular feedback is essential at every phase of the response.

Next, to understand how vestibular reflex pathways drive these postural responses in control animals, we recorded vestibulospinal neurons in the vestibular nuclei using a 32-channel probe and neural logger. Neural responses were observed at a significantly shorter latency than the onset of head motion, closely matching the latency of head motion onset in the animal with bilateral vestibular loss. This discrepancy is likely attributable to an unexpected mismatch between vestibular and proprioceptive signals. Moreover, the directionality of this modulation matched the neurons' responses to whole body movements, consistent with the goal of moving the head to compensate for unexpected motion. Finally, 100ms after perturbation onset, we found that neurons demonstrated marked attenuation of their response, consistent the reafference suppression of head motion arising from voluntary behavior. Taken together, these findings thus support our initial hypothesis and, for the first time, directly demonstrate the temporal progression of the vestibulospinal pathway's contribution to postural control.

<u>1-C-40 - Aging and cognitive-motor challenge differentially modulate cortical motor contributions to</u> <u>standing balance control</u>

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Details

Older adults (OA) engage more cortical resources than younger adults (YA) to control balance, which may contribute to falls. Competing cognitive demands may prevent cortical resource allocation towards balance, yet how cortical engagement is modulated during balance is unclear. We hypothesized that difficult balance tasks engage motor cortical substrates that are shared for difficult cognitive tasks. Transcranial magnetic stimulation (TMS) can index motor cortical contributions by measuring cortical spinal excitability (CSE). But, CSE is not often assessed during cognitive-balance challenge, especially in OA. We used TMS and standing cognitive-balance dual-tasks to measure CSE as a function of balance and cognitive challenge in able-bodied YA and OA. We predicted CSE and cognitive-motor performance would increase with balance challenge but decrease with cognitive-balance challenge, particularly in OA, because cognitive and motor areas compete for cortical resources.

Data were collected on 18 YA (18-35 years) and 18 OA (60-85 years). TMS was delivered over M1 to measure CSE during seated, easy (quiet stance; QS) and difficult (narrow stance over foam; NS) balance tasks. Each balance task was performed alone (no cognitive task; NoCog), and during easy (Oback) and difficult (2back) cognitive tasks. CSE was assessed by peak-to-peak motor evoked potential (MEP)

amplitudes. Cognitive-motor task performance was assessed with center of pressure sway and n-back accuracy.

Consistent with our predictions, our results suggest that OA may recruit more corticomotor resources during balance challenge. Compared to QS, MEPs increased during NS in OA (β =-50.7±13.6, p<0.001) but not YA (β =23.2±12.2, p=0.16). Contrary to our prediction, in NS, MEPs decreased with cognitive challenge in YA (β =60.5±20.5, p=0.0096) but not OA (β =-33.2±23.1, p=0.39), which may reflect a switch to an automatic/subcortical balance control strategy in YA and continued reliance on a cortical strategy in OA. Conversely, MEPs increased with cognitive challenge while seated in YA (β =-59.5±20.4, p=0.01) and OA (β =-81.8±25.3, p=0.0038), which may reflect a global increase in excitability with attentional demands. Despite finding no behavioral dual-task effects, given there were dual-task differences on MEPs, our results indicate that changes in CSE may have helped participants maintain balance and cognitive function during dual-task challenge.

Our results suggest cognitive resources may differentially modulate CSE across age and cognitivebalance challenge. We found YA flexibly shifted to automatic balance control by reducing cortical engagement during cognitive-balance challenge. OA maintained reliance on cortical motor resources and were unable to shift to an automatic balance strategy as age impaired subcortical motor systems likely could not support balance alone. This work will inform the development of precision (p)rehabilitation strategies to maximize balance function and reduce falls.

D - Integrative Control of Movement

<u>1-D-41 - Dual-task walking uncovers distinctive EEG effects on encoding and retention stages of</u> working memory in healthy young adults: A Mobile Brain-Body Imaging (MoBI) study

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Details

Introduction: Working memory (WM) is an executive function that allows to temporarily encode, maintain and use information to carry on goal-oriented behaviors. However, the interactions of the underlying neural circuits of WM are not fully understood. Furthermore, dual tasking, such as walking while simultaneously executing a cognitive action has been shown to modify behavior, gait and neurophysiology. However, it is unknown how modifications in cognitive load when walking or sitting influence behavior and neural processes during a WM task. To our knowledge, no studies have utilized the MoBI technology to explore cognitive-motor interaction (CMI) and variations in cognitive load on WM. Our objective was to characterize the effects of CMI and changes in memory load on WM in healthy young adults. We hypothesize that the interaction between cognitive and motor systems will uncover unknown WM traits. Better understanding of WM neurophysiology and how it is modulated by walking in a healthy population can provide clues to later study those at risk of disease.

Methods: 34 neurotypical young adults (18 (52.9%) females and 16 (47.1%) males with a mean age 22.41 \pm 4.61 and 16.2 \pm 2.88 years of education) completed a Delayed Match-to-Sample task (DMTS) using congruent or incongruent colored words stimuli, while sitting or walking on a treadmill. MoBI was utilized to simultaneously obtain behavioral, high density electroencephalography and gait recordings. Demographic information and a baseline cognitive score (MoCA) were also obtained. Data were analyzed with Matlab^R.

Results: Participants had an overall accuracy d' = 3.9, with behavioral improvements when walking (d' sitting = 3.772 ± 0.647 , walking = 4.054 ± 0.654 , $t_{33} = 2.786$, P = 0.009, Cohen's d = 0.478) and a decrement when exposed to incongruent stimuli independent of the motor condition (d' congruent = 3.933 ± 0.523 , incongruent = 3.787 ± 0.696 , $t_{33} = 2.473$, P = 0.019, Cohen's d = 0.424). No interaction was found between motor condition and congruency. Stride length wasn't modified by dual tasking. EEG amplitude reductions were found between sitting and walking at frontal, central and parietal scalp regions, during the encoding (conflict resolution - N200 and detection and processing of information - P300) and the retention (delay) period of WM (walking-sitting Cluster based Monte-Carlo permutation test - $t_{33} \approx -3.38$, P = 0.0036). An amplitude increase was found at occipital and right and left parietal scalp regions during the retention period (walking-sitting Cluster based Monte-Carlo permutation test - $t_{33} \approx 2.45$, P = 0.0216).

Conclusion: CMI using the MoBI uncovered hidden characteristics of WM encoding and maintenance in a young healthy cohort. Changes were observed in behavior and spatiotemporal EEG amplitudes associated with conflict resolution, detection and processing of information and semantic rehearsal processes of WM whether sitting or walking.

<u>1-D-42 - Standing, and alternating sitting and standing, as better for task performance and visual attention than only sitting</u>

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Details

When individuals stand, they sway and therefore must maintain their balance. Based on the dual-task hypothesis, it is generally expected that task performance is worse when standing than when sitting. In fact, when performing an attention task, individuals are engaged in a dual task when standing and a single task when sitting. This is one reason that explains why individuals predominantly work in a seated position in desk-based jobs. In contrast, we hypothesized that the standing position – with feet placed side by side at shoulder width – would be associated with better task performance and/or greater visual attention compared to the sitting-only position when performing an Attention Network Task (ANT). We further hypothesized that task performance and/or visual attention would be better/higher when alternating body positions six times in six trials than in the sitting-only condition. Indirectly, therefore, we hypothesized that task performance when using a sit-stand desk may be better than when using a traditional (sitting) desk. These hypotheses were based on recent published findings showing significantly better performance in the ANT and a modified Stroop task when standing than when sitting. Twenty-four healthy young adults (aged 18–35) performed the ANT six times in either the alternating condition or the sitting-only condition. In both between-condition and within-condition analyses, reaction times were significantly shorter when standing than when sitting. Furthermore, the proportion of blinks was significantly lower in the alternating condition compared to the sitting-only condition. Overall, humans may exhibit greater efficiency (i.e., shorter reaction times) and enhanced visual attention (i.e., less frequent blinking) in an alternating condition compared to a sitting-only condition. At a theoretical level, on the one hand, there is no doubt that individuals use fewer attentional resources when standing than when sitting. On the other hand, based on arguments discussed in the attention framework of Chajut and Algom (2003), individuals may better focus their selective attention when standing than when sitting. This improved attention selection when standing may be so efficient that it not only compensates for the reduced attentional resources available when standing compared to sitting, but it enables individuals to perform attention-demanding tasks better when standing than when sitting. In practice, the use of sit-stand desks may effectively help improve task performance by allowing individuals to spend time in the standing position in alternating between sitting and standing while working.

1-D-43 - The superior colliculus directs goal-oriented forelimb movements

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Details

Skilled forelimb control is essential for daily living, yet our understanding of its neural mechanisms, although extensive, remains incomplete. We present evidence that the superior colliculus (SC), a major midbrain structure, is necessary for accurate forelimb reaching in mice. We found that neurons in the lateral SC are active during goal-directed reaching, and by employing chemogenetic and phase-specific optogenetic silencing of these neurons, we show that the SC causally facilitates reach accuracy. Anatomical studies identified the deep cerebellar nuclei and substantia nigra pars reticulata as sources of inputs to the SC, while functional studies revealed a role for nigrotectal, but not cerebellotectal, neurons in controlling reach end- points. Silencing the nigrotectal pathway caused paw deviations opposite to those seen with SC silencing, emphasizing the coordinated role of the substantia nigra and SC in regulating optimal reaching. Together, these findings establish the SC as a crucial regulator of skilled forelimb control.

1-D-44 - The role of trajectory prediction in juggling

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<u>Details</u>

Interception is a fundamental aspect of daily activities, such as catching a moving ball in various sports. In ball-catching tasks, the endpoint of a movement can lie anywhere along the target's trajectory. Toss juggling exemplifies a motor skill that requires rhythmic catching and throwing of objects under spatial and temporal constraints. The planning and initiation of the catching action temporally overlaps with previous act of throwing the ball already in hand. A juggler's hand begins moving towards the catch location even before fully estimating the target's trajectory, requiring later adjustments to the targeted position during the movement. In our study, we determine the moment when the hand starts to follow a smooth path towards the catching region as a proxy for the termination of planning processes for the first ballistic approaching movement to the catching position. Particularly, we want to examine, whether movement planning is terminated earlier, if proprioceptive information from the previous toss is available.

Eighteen jugglers participated in the experiment. They were selected based on their ability to juggle a 3ball cascade for over 20 seconds. All jugglers were either right-handed or ambidextrous. The experiment had two conditions: solo and dyadic juggling. In the first, participants juggled a regular 3-ball cascade; in the second, they juggled with a partner. In dyadic juggling, two jugglers stood side by side: the left juggler (partner) used their left hand, the other (initiator) used their right, and they switched roles each trial. No instructions were given on speed or height. The study examined how a priori information on a ball's trajectory due to proprioceptive information and predictions based on efference copy from the throwing hand affected catching movements. We compared hand movements in solo vs. dyadic juggling, where throw information from the opposite hand was missing. Using the method proposed in [1], we examined how predictions based on information from the throwing hand affects the timing of the catching hand's movements. By leveraging the empirical principle that goal-directed trajectories exhibit minimal jerk, we evaluated how early jugglers' hand trajectories satisfy this smoothness criterion.

Our preliminary findings align with our hypothesis, demonstrating that jugglers can predict a ball's trajectory earlier when they have proprioceptive feedback from the throwing hand (solo juggling). In contrast, their ability to anticipate the trajectory is reduced when this information is unavailable (dyadic juggling). This highlights the critical role of sensory information from the throwing hand in facilitating early prediction and coordination during juggling.

Reference:

[1] Slupinski, L., de Lussanet, M. H., & Wagner, H. (2018). Analyzing the kinematics of hand movements in catching tasks—An online correction analysis of movement toward the target's trajectory. Behavior Research Methods, 50(6), 2316-2324.

1-D-45 - Neural contributions to abstract and motor task sequences

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<u>Details</u>

Humans complete sequences of tasks as a part of everyday life. Such sequences can be conceptualized as two types: those that are abstract, in which individual steps unfold according to a rule at second to minute-long timescales, and those that are motor, defined solely by individual movements and their order, which unfold at sub-second timescales. For example, the sequence of baking a cake consists of abstract tasks (such as adding the dry ingredients) and nested motor actions (such as whisking). Although motor and abstract sequences often co-occur, it is unclear if their execution is supported by the same cortical neural dynamics. Previous work highlights the importance of ramping dynamics (the increase of activity across sequences) in the rostrolateral prefrontal cortex (RLPFC) during abstract sequence execution (Desrochers et al., 2015), but the role of RLPFC dynamics during motor sequences was unknown. We tested the hypothesis that RLPFC ramping may generalize to support the execution of both sequence types by analyzing two functional magnetic resonance imaging (fMRI) datasets, one utilizing an abstract (Desrochers et al., 2015) and one a strictly motor sequence task (Yewbrey et al., 2023). In the abstract task, participants used a four-item sequence to make categorical choices about the color and shape of stimuli at each individual trial. Importantly, the tasks in these sequences did not rely on specific motor actions to complete. In the motor task, participants learned to perform four 5-finger key press sequences from memory when cued. We investigated ramping dynamics during sequence production in each of the tasks.

Overall, we found there was no significant RLPFC ramping during motor sequences, but ramping in bilateral regions of the inferior parietal cortex occurred during motor (in the AGRamp ROI) and not during abstract sequences (F(1,49) = 43.56, p < 0.001, η^2 = 0.47). Further analyses showed that ramping in specific subregions of inferior parietal cortex supported abstract compared to motor sequence production. We therefore show evidence that ramping dynamics dissociate these sequence types between the RLPFC and subregions of the inferior parietal cortex.

Our work shows evidence for differential neural circuitry underlying motor versus abstract sequences, implicating clinical disorders that may involve both motor and cognitive deficits, such as obsessive-compulsive disorder (OCD). We show additional evidence using the same abstract sequence task (Desrochers et al., 2015) that ramping in the AGRamp ROI (region of significant ramping during motor sequence execution) dissociates OCD from healthy controls, suggesting there may be an imbalance in the recruitment of cortical regions that support motor versus abstract task sequences in this disorder. This work prompts future studies to investigate the neural integration of these sequence types when they co-occur, both in healthy individuals and psychiatric populations.

1-D-46 - Finger tapping at maximal speed evokes a Crossover-Fatigability effect

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<u>Details</u>

Introduction

Crossover-fatigability (CF) is a phenomenon that describes a fatiguing effect of one effector on the homologous unfatigued effector that has not been involved in the movement. Whether CF can be robustly evoked is still debated and thus the knowledge of the underlying mechanisms is still limited. Here, we use a rapid finger-tapping paradigm to induce fatigability and to detect the existence of a CF effect. Fatigability is assessed through motor slowing, a decrease in movement speed that occurs when maximal tapping speed cannot be maintained. Motor slowing has been associated with predominantly supraspinal mechanism, making it a suitable model to explore the supraspinal involvement in CF. In this study, we aimed to determine whether CF can be induced using motor slowing, which may indicate that CF is mediated by supraspinal mechanisms.

Method

30 participants (24 +/- 4y, 17 female) performed finger tapping at maximal voluntary speed with their index fingers. The task consisted of tapping with one hand (*Pre*) for 10s (resulting in *control*) or 30s (resulting in *CF*) followed immediately by tapping with the other hand (*Post*) for 30s. The starting hand was either the dominant (DH) or the non-dominant (NDH), resulting in 4 experimental conditions, which were pseudorandomised throughout the experiment with 6 trials each. The tapping data was averaged into 10s bins. Statistical analyses were performed using linear mixed-effects models with random intercepts of participants and interaction of all factors. We tested for (i) the magnitude of the CF effect (percentage change in tapping speed from bin 1 of *Pre* to bin 1 of *Post*, calculated separately for each hand) in dependence of *Condition* (CF, control) and *Hand* (DH, NDH), and (ii) the extent of motor slowing (percentage decrease in tapping speed from time bin 1 to bin 3) in dependence of *Condition* (pre, control, CF) and *Hand* (DH, NDH). Note that for pre, only the 30s conditions were used.

Results

We indeed found CF to be present, as the tapping speed was lower in the *CF* condition compared to the *control* condition (significant main effect of *Condition* of model i, *p*<.001). Further, we found that motor slowing in the second hand was reduced compared to the first hand (significant main effect of *Condition* of model ii, *p*<.001). Additionally, we found that the DH showed significantly less extent of motor slowing (9.1 +/- 0.5%) than the NDH (11.8 +/- 0.6%, main effect of *Hand*, *p*<.001).

Conclusion

We show that CF can be evoked using a fatiguing finger-tapping task. This CF effect was observed as a reduced tapping speed of the second hand. Also, we found that the decrease in movement speed is reduced if the first hand performed even 10s of finger tapping. Thus, 10s of maximal speed finger tapping may already be enough to induce a change in the fatiguing behaviour of the second hand. As motor slowing is a phenomenon predominantly associated with supraspinal mechanisms, we propose that CF may be mediated supraspinally.

<u>1-D-47 - Effects of Cervical tSCS at sub-motor thresholds on force proprioception and motoneuron</u> <u>activity</u>

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<u>Details</u>

Transcutaneous spinal cord stimulation (tSCS) has emerged as a promising non-invasive neuromodulatory technique for enhancing motor recovery in individuals with spinal cord injury (SCI). By modulating spinal cord neural activity, tSCS may enhance sensory processing, promote neuroplasticity, and improve limb function. When applied at sub-motor threshold intensities, it has shown encouraging results in restoring hand and arm function, though the underlying mechanisms remain unclear.

While most studies have focused on the short-term post-stimulation effects of tSCS, fewer have investigated its immediate impact on motoneuron activity during stimulation. Understanding these acute neuromodulatory effects is essential for designing targeted stimulation protocols that optimize functional improvements in different disorders. This study aimed to characterize the effects of submotor threshold cervical tSCS on force proprioception and motoneuron activity in upper limb muscles of healthy individuals, using state-of-the-art intramuscular electromyography (iEMG) acquisition and decomposition techniques.

iEMG was recorded from the flexor carpi radialis (FCR) muscle during 15% maximal voluntary contraction (MVC) steady isometric contractions. Participants received cervical tSCS over the C6-T1 spinal segments, applied below motor threshold, while tracking and maintaining their force output during wrist flexion with and without visual feedback. Multiple stimulation conditions, including various frequencies and a baseline (no stimulation), were assessed. Motor unit properties—firing rate, recruitment and de-recruitment thresholds—were analyzed and compared across conditions. Additionally, the force profile was examined to assess the impact of stimulation on proprioception and motor performance.

Preliminary results indicate that tSCS influences force proprioception. During tSCS, participants exhibited increased force output in the absence of visual feedback compared to baseline (p<0.05) but were able to compensate when visual feedback was available. However, the root mean square error (RMSE) during tSCS and sham stimulation (trapezius) was similar, suggesting that the observed effects on force proprioception may be indirect and related to cognitive distraction rather than direct neuromodulation.

This study provides novel insights into the acute effects of cervical tSCS on upper-limb motor unit activity using iEMG in healthy individuals. The findings contribute to the refinement of tSCS protocols, potentially improving motor rehabilitation strategies and functional outcomes for individuals with SCI and other motor impairments.

<u>1-D-50 - Modulation of corticospinal excitability in an upper-limb obstacle-avoidance reaching task</u> Justin Mccurdy ¹, Haleh Mahmoudi ¹, Brendan Jarvis ¹, Deborah Barany ¹

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Details

To efficiently reach around visual obstacles in our environment, humans must plan both the spatial goal and the movement trajectory. Planning a specific movement trajectory is thought to contribute to slower reaction times (RTs) for movements around obstacles relative to simpler, point-to-point reaching movements. However, it is unknown how the motor system modulates its output to support trajectory planning during obstacle-avoidance movements. Here, we combine transcranial magnetic stimulation (TMS), multi-muscle electromyography (EMG) recordings, and a two-dimensional upper-limb reaching task to investigate how corticospinal excitability is modulated while preparing obstacle-avoidance reaches. Twenty-four neurologically healthy, right-handed participants (13 F, age 20.5 ± 1.79 years) performed a reaching task using a KINARM End-Point robotic manipulandum with their right hand. On each trial, participants were required to reach from a start target to a goal target while avoiding hitting obstacles impeding a straight-line movement path. All visual stimuli disappeared at movement onset to discourage online planning. In the Cued blocks, the optimal movement path was provided to alleviate planning demands, whereas in the Non-Cued blocks, no guidance was given. Motor-evoked potentials (MEPs) were elicited in response to TMS applied over the extensor carpi radialis (ECR) representation of primary motor cortex at one of three timepoints relative to the participant's median RT from the no-TMS blocks. During TMS blocks, RTs were significantly longer for Non-Cued trials (p = 0.02), and shorter when TMS was applied earlier in the preparation period (p < 0.001). Relative to in-task baseline MEP amplitude, MEP amplitudes during the preparation period were significantly enhanced for both ECR (p < 1(0.001) and flexor carpi radialis (p = 0.003) muscles, especially when applied closer to movement onset. Interestingly, there was greater facilitation in the ECR muscle for Cued relative to Non-Cued trials at the closest timepoint to movement onset (p = 0.03) suggesting that slower RTs in this condition are related to a slower ramping of preparatory activity when more complex trajectory planning is required. Together, these results provide initial evidence that planning complex movement trajectories modulates corticospinal excitability and provide novel insight into how corticospinal circuits may be differentially engaged during complex, goal-directed reaching behavior.

<u>1-D-51 - Enhanced muscle activity during jumping behavior in tendon-specific Piezo1 gain of function</u> <u>mice</u>

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<u>Details</u>

Tendons are strong tissues that connect muscle and bone, and tendon properties and strength are known to be related to muscle strength, such as increased muscle output and stabilization. However, the relationship between muscle activity and tendon is not clear. We have shown that a gain-of-function mutation in Piezo1, a mechano-stimuli-responsive channel, was introduced specifically into mouse tendons and increased locomotor function, including jumping ability. No histological changes in muscle were observed in these mice, suggesting the possibility of a new motor control mechanism that enhances muscle activity originating from tendons. In the present study, we evaluated the relationship between tendon and muscle activity by performing EMG measurements during jumping in wild-type (WT) and tendon-specific Piezo1 gain-of-function (GOF) mice and comparing the results.

In the experiment, electrode implantation surgery was performed under general anesthesia for WT and GOF, respectively. Wire electrodes were implanted in the lower leg muscles of the mice (tibialis anterior and gastrocnemius muscles) and the connectors were fixed to the head.

Electromyograms during jumping were recorded on the third postoperative day.

A cage 50 cm wide, 25 cm deep, and 15 cm high was placed on a table 80 cm high. A 3 cm wide beam was placed 5 cm from the cage, and the mouse was placed on the beam. Mice were moved into the cage by pointing them toward the cage and stimulating their tails and rumps by touch. 5-cm movement was successfully completed, then the beam was moved away from the cage step by step and the mice learned to move by jumping by repeated movement. After learning, we connected a recording cable to the head connector and measured electromyograms during jumping. The distance between the cage and the beam was set in 5-cm increments, and 10 EMG recordings were made for jumps of 15 cm, 25 cm, and 35 cm, respectively. Jumping movements were recorded with a high-speed camera and evaluated in synchronization with electromyography. After the jump experiment, we electrically stimulated the sciatic nerve with needle electrodes under general anesthesia, and the EMG during the jump was normalized. Comparison between groups of WT and GOF mice was conducted based on the above recorded data.

Both WT and GOF showed a peak in the lower leg EMG just before takeoff (-0.05s). No jumpingdistance-dependent changes were observed in the tibialis anterior muscle, but they were observed in the gastrocnemius muscle, confirming that the gastrocnemius muscle is active as one of the main muscles during the jumping movement. Comparison of EMG of the gastrocnemius muscle between groups showed greater amplitude in the GOF than in the WT. These results suggest a link between tendon and muscle activity.

1-D-52 - Connectome-based modelling reveals a core brain network predicting hand motor behaviour

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<u>Details</u>

Introduction. Hand motor behavior arises from complex interactions within a widespread brain network. It has been proposed that behavioral performance is also represented in "intrinsic" – i.e., non-task related - brain connectivity. Here, we tested whether resting-state functional connectivity (rs-FC) within this network could predict hand motor behavior. We applied connectome-based Predictive Modeling (CPM) to predict individual behavioral measures from rs-FC. Our goals were: 1) identifying a

"core" hand motor network; 2) testing its predictive power on motor variables; and 3) testing the generalization of its predictive power on an independent dataset.

Methods. We analyzed rs-fMRI and behavioral data from 969 right-handed participants of the Human Connectome Project. We considered two behavioral measures: 1) hand dexterity and 2) upper limb strength, separately for the right (RH) and left (LH) hands.

Support Vector Regression (SVR) was applied to whole-brain rs-FC to predict these variables separately. Predictive power was assessed via Pearson Correlation between observed and predicted behavioral values. Three of the four whole brain CPM models showed a significant prediction power: dexterity for RH, strength for LH, and for RH (p < 0.005 FDR corrected). We identified a "core" hand motor network as the intersection of significant connections across these three models.

Then, we tested if our core network could capture specific and more general aspects of hand motor behavior. Using SVR, we examined whether a CPM model trained on a specific motor variable (e.g., LH force) could predict: 1) a different variable within the same dataset (e.g., LH dexterity) and 2) a different variable on an independent rs-fMRI and behavioral dataset.

Results. CPM whole-brain models (~60.000 connections) significantly predicted dexterity for RH and strength for LH/RH. We identified a "core" hand motor network with fewer connections (~1.800) - which had similar predictive power for the same behavioral variables. The core hand motor network comprises areas of the Dorsomedial, Dorsolateral, and Ventral visual pathways (Middle and Inferior temporal lobe) and of the Cerebellum.

Additionally, CPMs based on the core network captured broader aspects of hand motor behavior, predicting: 1) the same task performed with a different hand; 2) a different task performed with the same hand; 3) a different task performed with a different hand. Finally, the core network model successfully predicted hand motor features from an external independent dataset.

Discussion. We identified a core network that predicts motor variables from rs-FC, suggesting that information about hand motor behavior is also represented in "intrinsic" brain connectivity and that this network represents higher-order aspects of hand motor control. This network offers a valuable target for studies investigating causal links between brain activity and motor function (e.g., TMS).

1-D-53 - All sensory-to-motor pathways through the Drosophila central nervous system

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<u>Details</u>

Coordinated motor control requires the brain to engage with local circuits in the spinal cord or, in insects, the ventral nerve cord. Meanwhile, the spinal cord and ventral nerve cord relay feedback from ongoing motor behaviors back to the brain. These loops form the basis of motor control. However, the detailed connectivity of these loops is not well understood. Here we describe for the first time a full connectome of the *Drosophila* central nervous system (called the *Drosophila* Brain And Nerve Cord, or BANC), and we use this resource to establish the full wiring diagram of these motor control loops within

the nervous system. In *Drosophila* this top down control is exerted through descending neurons, i.e. neurons that project from the brain to the ventral nerve cord, while the feedback is transmitted through ascending neurons, or neurons that project from the ventral nerve cord up to the brain. We have developed a taxonomy of ascending and descending neurons based on morphology and connectivity. Moreover, we have assigned putative behavioral roles to many uncharacterized ascending and descending neuron types based on their detailed connectivity. To achieve this, we developed a simulation method based on a linear dynamical model of firing rate propagation across the connectome following modeled external stimulation of any given neuron or set of neurons (seeds). This allowed us to quantify indirect influence of sensory and motor neurons on each ascending and descending neuron type. We have identified novel circuits for the control of walking, flight, landing, grooming, and reproductive behaviors. Our results reveal subcircuits that coordinate movements in flight. This new open-access public resource will allow detailed investigations of the neuronal circuits underlying the control of diverse motor patterns in *Drosophila*. More broadly, this data set illustrates interesting principles underlying the integration of top-down commands, local central pattern generators, and sensory feedback in the control of movement.

1-D-54 - Stability of rhythmic movements in the face of dynamic, cognitive and perceptual interactions

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Details

Much previous work on rhythmic movements has shown a preference for certain frequencies in humans and animals. For finger movements, the ubiquitous preference is close to 2Hz, similar to the perception of musical rhythms. For pendulum-like movements of the inertial limbs, such as in locomotion, the preferred rates are close to the resonance frequency of pendular models of the moving limbs. While the latter provides evidence that humans exploit the dynamic properties of their limbs, little attention has been given to inter-individual differences in such behavior and potential interactions with other properties and task demands, including rhythm perception.

Rhythmic motion in bimanual coordination has been successfully understood as limit-cycle attractors of nonlinear oscillators. The stability of such oscillators depends on dynamic parameters that may vary between individuals, such as age or music training, but also muscle stiffness. Cognitive load has also been reported to affect the stability of phase coupling between two limbs. Furthermore, interactions between control and perception of rhythms are suggested by the involvement of motor cortical areas during listening to music.

Three different experiments scrutinized how different factors affect the stability of rhythm production and perception. A first field experiment used the traditional finger tapping task and tested over 200 subjects aged 5 to 92 yrs. Results showed that period and variability of the rhythmic movements were modulated by age and music training. When deflected from their preferred tempo, the period drifted towards the spontaneous motor tempo, indicating the presence of a stable limit-cycle attractor. In the second experiment, subjects oscillated their wrist while holding one of two pendulums, counting backwards aloud. Results showed that subjects adopted rhythms close to the natural frequency of the pendula. Small but consistent inter-individual differences in their chosen tempi remained stable over 10 days, both for swinging alone and with the cognitive task. Cognitive processes significantly impacted the period of the movements in an individual-specific fashion. Grip force was modulated in synchrony with the cyclic wrist movements and the voicing of the cognitive task. A third experiment tested whether rhythmic motor practice could influence beat perception. Five days of training at bouncing a ball at the preferred tempo was followed by a temporal acuity test. Counter to expectations, preliminary results showed only negligible effects on temporal discrimination.

These results highlight that stability of the oscillatory dynamics of rhythmic movements, shaped by the mechanical limb properties, affects short-term and long-term rhythmic behavior. Together with evidence of synchronization between speech and movements, these results suggest interesting interplay between motor and cognitive processes in rhythmic behavior, while remaining separate from subsequent beat perception.

<u>1-D-55 - A quantitative, physiologically-meaningful breakdown of the constituent components of the brain and kinematic responses to environmental events reveals causal relationships between neural activity and motor responsiveness</u>

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<u>Details</u>

Salient and unexpected sensory stimuli likely to signal environmental events that require immediate reactions evoke large electrocortical transients that modulate corticospinal output. After having characterised the effect of these stimuli on isometric force in human and non-human primates, in recent experiments we asked (1) whether the same salient stimuli also elicit whole-body movements when human participants maintain an unconstrained, natural posture, and (2) what is the causal relationship between the constituent components of the large electrocortical response and of the motor responses. Human participants received fast-rising intensity-matched acoustic and somatic stimuli, delivered to either the left or the right side, with modality and position intermixed. Stimuli had high intensity and long and variable intervals. High-resolution kinematic data and high-density electroencephalographic data (EEG) were collected simultaneously. We devised a novel analytical approach that combines spatiotemporal principal component analysis (stPCA) with linear discriminant analysis (LDA), to reduce the dimensionality of complex kinematic data and identify behaviourally meaningful movement constituent components (MCCs) not detectable through conventional analysis techniques. The same dimensionality reduction was applied to the electrocortical responses elicited by the sensory stimuli within different experimental conditions.

We demonstrated unique MCCs from the kinematic response. These were a composition of modalitydependent, modality-invariant, location-dependent, and location-invariant MCCs, which combined identified behaviourally-significant movements (e.g. startle, orienting, avoiding). Specifically, (1) somatic stimuli elicited a fast, spatially-oriented limb withdrawal, followed by a slower and more global avoidance movement of the trunk and head. In contrast, (2) auditory stimuli did not cause the fast withdrawal but only showed the global avoidance movement. (3) All stimuli elicited a startle-like, nonspatially oriented movement, invariant to stimulus modality and location.

We confirmed the previously-described brain constituent components (BCCs) of the EEG response to salient stimuli. This response was dominated by BCCs invariant to stimulus modality and location, reflecting processes mediated by diffuse 'extralemniscal' thalamocortical projections. In contrast,

modality-specific 'lemniscal' processes limited to primary sensory cortices were isolated in BCCs contributing to a small and early part of the response. Crucially, the dominant supramodal, extralemniscal brain component causally determined the startle-like, non-spatially oriented movement, without having a major role in the spatially-oriented, avoidance response.

This is the first breakdown of the motor constituent components (MCCs) of the kinematic response to salient environmental stimuli, indicating a clear primacy of defensive rather than approaching behaviour, and the first demonstration of a causal relationship between the large and widespread thalamocortical activity and the startle response. This novel approach opens a powerful opportunity to investigate how neural activity causally relates to the building blocks of natural motor behaviour.

E – Disorders of Motor Control

1-E-56 - Effects of exercise therapy on cerebellar activity in cervical dystonia

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Details

Cervical dystonia (CD), the most common type of focal dystonia, is characterized by abnormal and repetitive head and neck movements. Current treatments, including oral medications, botulinum toxin injections, and deep brain stimulation surgery, often fail to improve symptoms in over one-third of patients, even with optimal management. Recent studies suggest that exercise therapy, involving muscle stretching, muscle relaxation, and range-of-motion exercises, can further improve symptoms of focal cervical dystonia when combined with medical care. However, little is known about how such physical therapy interventions affect brain function, particularly in regions implicated in motor control.

In this study, we investigated the effects of physical therapy programs, specifically progressive resistance exercises for upper body muscles in individuals with CD using a task-based functional magnetic resonance imaging (fMRI) protocol. Although CD is traditionally classified as a basal ganglia disorder, it is increasingly recognized as a network disorder involving other interconnected areas, especially the cerebellum. Given the cerebellum's critical role in motor coordination and sensorimotor integration, we focused our analysis on cerebellar activity.

Forty patients with CD (32 females, 8 males) were randomized into two groups: one group participated in a structured, supervised physical therapy for six months, while the control group received standard of care. All participants underwent fMRI scans at baseline (Visit 1) and after six-month follow-up (Visit 2). A voxel-based analysis was used to compare changes in brain activity between the groups.

The whole brain analysis revealed functional changes in clusters in the cerebellum. Subsequent cerebellum-focused analysis was performed using SUIT (SPM12) toolbox. Results revealed a trend of increased cerebellar activation in the control group at Visit 2, particularly in regions associated with motor coordination. In contrast, the physical therapy group exhibited a significant reduction in activity in cerebellar lobule V, lobule VI, and Crus I— areas known for their critical role in sensorimotor integration and motor planning. Our findings underscore the role of cerebellum in the pathogenesis of dystonia.

These findings highlight the critical role of cerebellum in the pathogenesis of dystonia. It may suggest that the therapy-based progressive resistance exercise could effectively reduce cerebellar hyperactivity in CD, potentially reflecting improved sensorimotor processing and more efficient motor control. The observed neuroplastic changes underscore the potential of therapy-based resistance exercise as a non-

invasive intervention to modulate brain activity in dystonia and enhance motor function in individuals with CD.

<u>1-E-57 - Reorganization of the cortical motor maps of multiple upper extremity muscles with</u> <u>rehabilitation therapy in stroke survivors</u>

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Details

The corticospinal tract integrity plays a vital role in motor recovery after stroke. Upper extremity movement requires coordinated control of multiple muscles. However, previous studies have only examined a single muscle and not considered corticospinal control of multiple muscles in stroke survivors. Knowledge regarding cortical spatial reorganization for multiple upper extremity muscles may inform optimal neuroplasticity for better clinical outcome.

The objective of this research aimed to investigate the impact of rehabilitation therapy on the cortical motor maps of multiple upper extremity muscles affected by stroke.

The preliminary analysis included 24 chronic stroke survivors (>6 months post-stroke) with moderate hand impairment (as indicated by the Wolf Motor Function Test (WMFT) times between 10 and 120 seconds for hand task items). Each participant underwent 18 sessions of upper limb therapy sessions with a physical or occupational therapist over 6 weeks. The motor maps of four muscles for the hand were assessed before and after the therapy. The muscles included: abductor pollicis brevis, first dorsal interossei, flexor digitorum superficialis, and extensor digitorum communis, all in the affected upper limb. The motor cortex was stimulated using transcranial magnetic stimulation (TMS) on a 5 cm x 5 cm grid over the primary motor cortex in the hemisphere affected by the stroke, at 110% of the resting motor threshold. Motor evoked potentials (MEPs) were obtained at each grid point for each muscle. The motor map was defined as the cortical area where TMS induced MEP of at least 0.05 uV with 50%+ probability for a given muscle.

The results showed that stroke survivors with higher upper extremity motor function tend to have larger cortical motor map sizes prior to receiving therapy across multiple upper extremity muscles. Those who achieved greater upper extremity motor recovery after therapy had an increase in the cortical motor map size.

This study showed that rehabilitation therapy induces motor map reorganization among multiple upper extremity muscles. An increase in the size of cortical motor maps for multiple upper extremity muscles appears to be beneficial for the paretic upper limb motor recovery. This finding highlights the organization of cortical neuroplasticity and motor control for multiple muscles needed for upper extremity motor function. This study provides insights into the corticospinal neuroplastic mechanisms of upper extremity motor recovery to spark development of innovative post-stroke rehabilitation treatments.

1-E-58 - Brain-heart interactions underlying movement disorder symptoms in Parkinson's disease

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<u>Details</u>

The interaction between the brain and interoceptive signals, such as heartbeats, plays a key role in maintaining internal balance and regulating neural dynamics, shaping cognition and behavior. Recent methodological advances suggest that examining the covariation between cardiac rhythms and the formation of functional brain networks offers a promising approach to understanding various dimensions of bodily self-awareness, including the sense of control over body movements.

Many pathologies manifest disruptions in brain-body interactions, making these physiological manifestations valuable biomarkers for diagnosing, monitoring, and predicting neurological disorder outcomes. Parkinson's disease, which affects neurons throughout the body, significantly impacts brainheart interactions. While these interactions have been linked to dysautonomia, our recent studies using non-invasive electrophysiology (EEG, ECG) in diverse cohorts demonstrate that brain-heart dynamics can effectively track motor symptoms, such as tremors and freezing of gait.

Using two distinct frameworks, we demonstrated that Parkinson's disease alters resting-state brain-heart physiology. Specifically, we identified distinctive couplings between cardiac rhythms and the dynamic formation of brain connections, as well as global measures of brain integration and segregation. Additionally, we tracked how these couplings change with and without dopaminergic therapy, revealing that the degree of coupling change correlates with motor symptom improvement. Expanding this research, we investigated brain-heart interactions during freezing of gait episodes, with preliminary results indicating that cardiac rhythmicity predicts these episodes. Our ongoing work aims to uncover links between heart activity and functional brain networks during these events.

Studying brain-heart interactions provides an integrative perspective that could enhance the accuracy of physiological evaluations. This research opens new avenues for targeted interventions, tailored to the specific physiological responses observed during neurorehabilitation procedures.

1-E-59 - Unimanual predictors of bimanual cooperative control in subacute stroke

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Details

Introduction. After a stroke, bimanual coordination is often impaired. Deficits in bimanual cooperative tasks are particularly prevalent, as precise spatiotemporal interaction between both hands is required for task execution success. Different underlying sensorimotor mechanisms may contribute to these deficits, including alterations in feedforward and feedback control, or proprioception. This study aimed to characterize unimanual sensorimotor impairments and assess their relative influence on bimanual cooperative control in subacute stroke.

Method. Thirty-six hemiparetic stroke survivors (64±14 years, 64±15 days post-stroke, 70% right hemisphere stroke) completed three standard tasks using a Kinarm Exoskeleton Lab. The first task was an unimanual target pointing task performed with the paretic upper extremity (Visually Guided Reaching). Metrics representing feedforward control (i.e., initial direction angle and initial distance ratio) and feedback control (i.e., speed maxima count and difference between local speed minima and maxima) were extracted. The second task was a bimanual cooperative task in which participants stabilized a ball on a bar held with both hands and reached for targets (Ball on Bar). Metrics representing interlimb difference (i.e., hand speed difference and hand speed peak bias) and bimanual coupling (i.e., bar tilt standard deviation and bar length variability) were extracted. The third task was a proprioceptive task (Arm Position Matching). All metrics were converted to Z-scores based on normative data from healthy subjects, accounting for age, gender, and hand dominance. Two stepwise multiple linear regression models were performed with interlimb difference or bimanual coupling as dependent variables and feedback impairment, feedforward impairment, proprioceptive impairment, and lesion side as potential independent variables.

Results. Assessment of unimanual sensorimotor control revealed impairments in 53% of stroke survivors for feedforward control, 28% for feedback control, and 33% for proprioception. Assessment of bimanual cooperative control revealed impairments in 42% for interlimb difference and 19% for bimanual coupling. Multiple linear regression showed that interlimb difference was best explained by unimanual feedforward impairment (R^2 =0.63; p<0.001). Bimanual coupling was better explained by feedback and proprioceptive impairment (R^2 =0.54; p<0.001).

Discussion. These findings suggest distinct contributions of specific unimanual sensorimotor impairments to different components of bimanual control. Interestingly, feedforward unimanual control of the paretic limb was strongly associated with interlimb difference, and both were the most prevalent types of deficits. Deficits in proprioception and feedback control were somewhat less common and were more predictive of bimanual coupling, i.e., the ability to maintain the position of the object held between both hands stable.

<u>1-E-60 - The contribution of ipsilesional premotor and somatosensory cortex on skilled forelimb use</u> <u>after a unilateral ischemic injury to primary motor cortex in the rat</u>

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Details

Stroke is one of the major contributors to chronic motor impairments worldwide. The extent of these impairments is likely due to a combination of a direct loss of neurons at the site of injury that contribute to the execution of movement as well as the disruption of communication across spared regions. Following injury, some restitution of function can occur either spontaneously or in response to rehabilitative therapies. While large-scale reorganization has been shown within and between spared cortical areas and is thought to contribute to recovery, the precise role these areas have in contributing to motor function after the injury is not well established. To understand the role of these spared areas during motor recovery, we wanted to address three main questions: 1) Is task-related neural encoding disrupted by a focal ischemic lesion within the sensorimotor network? 2) Is behavioral recovery associated with a restoration or reestablishment of neural population dynamics? 3) Are increases in sensorimotor integration between spared areas related to recovery? In a within-subjects design, 12 Long-Evans rats were trained to perform a skilled pellet retrieval task prior to having chronic, 32-channel microelectrode arrays implanted into unilateral premotor and primary somatosensory cortex. Neural data was recorded during the task prior to and following a focal ischemic infarct to primary motor cortex. Single-unit data were extracted and aligned to the grasp phase of the reaching task. Task-related neural population dynamics were estimated using Gaussian Process Factor Analysis (GPFA) and quantified using trajectory length, dispersion, and alignment to compare the neural response across
different behavioral sessions. Prior to injury, stereotypical task-related neural trajectories were observed. Immediately following injury, these trajectories were significantly disrupted, with the degree of disruption correlated to the amount of observed motor deficit. Task-related modulation of shared premotor-somatosensory activity was calculated using canonical correlation analysis (CCA) and quantified using d'. The injury resulted in an increase in correlated activity between the two regions, but a significant decrease in task-related modulation. These results indicate that the task-related motor encoding within premotor and somatosensory cortex are not static after an injury and further reinforce importance of spared cortical networks in motor recovery.

<u>1-E-61 - Understanding nicotine dependence through bimanual force control performance in chronic</u> <u>smokers</u>

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<u>Details</u>

Background: Chronic smoking is the leading cause of various neurological disorders, including stroke and Alzheimer's disease. Despite many chronic smokers attempting to quit, the majority fail due to withdrawal symptoms. Loss of motor control during smoking cessation is a potential withdrawal symptom disrupting activities of daily living and hinders successful quitting. Various motor assessments indicated impaired coordinative upper limb movement due to the synaptic changes caused by chronic smoking. Providing quantitative evidence of potential benefits in activities of daily living in chronic smokers can enhance our understanding of nicotine-dependent aspects in chronic smokers with behavioral approaches and to highlight the importance of motor rehabilitation in supporting smoking cessation.

Objective: This study aimed to investigate the effects of nicotine on bimanual motor control by comparing the force control capabilities in chronic smokers and non-smokers.

Methods: A total of 34 subjects (17 chronic smokers and 17 age-matched non-smokers) participated in this study. Using an isometric force control paradigm, participants performed bimanual isometric force control tasks at 10% of maximum voluntary contraction. The outcome measures included force accuracy (root-mean-squared error; RMSE), variability (standard deviation; SD), bimanual coordination (correlation coefficient; r), and bilateral synergies (V_{UCM}). Independent t-test analyzed the difference between the groups across the outcome measures.

Results: We revealed that transient improvements in bimanual force control performance as indicated by less force error and variability appeared in chronic smokers than non-smokers, whereas both groups showed similar interlimb coordination patterns. These findings suggested that the transient benefits of nicotine on bimanual force control functions in chronic smokers contribute to addictive behaviors in smoking.

Conclusion: The current study identifies that nicotine-induced motor improvement is a potential risk factor for nicotine dependence in chronic smokers, based on bimanual force control functions. Future studies should investigate force control pattern changes in chronic smokers under different nicotine conditions to improve the validity of these findings.

1-E-62 - The impact of synaptic dynamics on the efficacy of neurostimulation technologies

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Details

Electrical stimulation of the nervous system is a growing field of research with the potential to greatly improve the quality of life of patients suffering from motor control disorders. Epidural spinal cord stimulation (SCS) is one of these novel therapeutic techniques, promising to dramatically help patients regain voluntary motor control. In epidural SCS, electrode leads lay on top of the bundle of fibers that compose the spinal cord, applying electrical current to modulate the activity of these nerves. It is believed that SCS functions by activating proprioceptive afferent fibers in the dorsal column of the spinal cord, which in turn convey this excitation to motoneurons via a mono-synaptic connection (Seáñez & Capogrosso, 2021). Within the motoneuron, this input summates with the remaining weak descending inputs, resulting in volitional movement (Balaguer et al., 2024).

Although it is widely accepted that the afferent-motoneuron synapse plays a crucial role in the efficacy of SCS for movement disorders, the details of synaptic transmission from SCS-induced afferent firing to motoneuron response are often overlooked. Specifically, it is known that repetitive stimulation can deplete the available neurotransmitter in the afferent fibers, resulting in progressively smaller responses in the motoneuron at higher stimulation frequencies (Wan et al., 2006). This phenomenon, known as rate-dependent depression (RDD), restricts the transmission of stimulation from the afferent fibers to the motoneuron, thereby imposing a potential limitation of SCS. Here, we consider the role that ratedependent depression (RDD) plays in determining the efficacy of SCS and explore methods for optimizing stimulation using models of RDD in spinal circuitry. We quantify spinal RDD in non-human primates and human patients implanted with SCS by using electromyography (EMG) to measure the depression in muscle responses evoked by direct stimulation of afferent fibers at a range of stimulation frequencies. We also evaluate RDD in healthy control participants by comparing the depression of the Hoffman-reflex (H-reflex)-a reflex triggered non-invasively through the same afferent-motoneuron spinal synapse–across stimulation frequencies. Next, we develop a computational model of RDD in spinal circuitry and fit it to our experimental data, allowing us to systematically explore the parameter space of stimulation. Using this model, we predict paradigms that minimize synaptic depletion and optimize the transmission of stimulation, such as bursts of stimulation and amplitude modulation during stimulation trains. We test these SCS paradigms in non-human primates and human subjects in order to determine which parameters result in the largest increases of evoked-EMG responses across the stimulation window compared to the same timeframe of continuous SCS. Ultimately, this project evaluates the role of synaptic dynamics in limiting transmission of stimulation and proposes methodology to optimize stimulation given this restriction. While this project focuses on SCS, its implications extend far beyond, as understanding synaptic transmission is essential for optimizing the targeted responses to electrical modulation across all forms of neurostimulation technologies.

<u>1-E-63 - Aberrant motor planning and preparation of hand movement in schizophrenia spectrum</u> <u>disorder: An fMRI study</u>

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<u>Details</u>

Schizophrenia spectrum disorder (SSD) is linked to impaired self-other distinction and action feedback monitoring, largely stemming from sensory-motor predictive mechanisms. However, the neural correlates of these predictive processes during movement preparation are unknown. Here, we investigated whether patients with SSD exhibit aberrant sensory-motor predictive processes reflected in neural activation patterns prior to hand movement onset. Functional MRI data from patients with SSD (n = 20) and healthy controls (n = 20) were acquired during actively performed or passively induced hand movements. The task required participants to detect temporal delays between their movements and video feedback, which either displayed their own (self) or someone else's (other) hand moving in accordance with their own hand movements.

Patients compared to healthy controls showed reduced preparatory blood-oxygen-level-dependent activation (active > passive) in clusters comprising the left putamen, left insula, left thalamus, and lobule VIII of the right cerebellum. Reduced activation in the left insula and putamen was specific to own-hand feedback. Additionally, patients with SSD revealed reduced suppression (passive > active) in bilateral and medial parietal (including the right angular gyrus) and occipital areas, the right postcentral gyrus, cerebellum crus I, as well as the left medial superior frontal gyrus. Ego-disturbances were negatively correlated with left insula and putamen activation during active conditions, and with right angular gyrus activation patterns during passive conditions when own-hand feedback was presented.

These findings suggest that group differences are primarily evident during preparatory processes. Our results show that this preparatory neural activation is further linked to symptom severity, supporting the idea that the preparation of upcoming events as internal predictive mechanisms may underlie severe symptoms in patients with SSD. These findings could improve our understanding of other deficits in action planning, self-monitoring, and motor dysfunction in various psychiatric, neurological, and neurodegenerative disorders.

<u>1-E-64 - Inconsistencies among neurophysiological, matching and metacognitive data on</u> <u>proprioception</u>

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Details

Although it is well established that proprioception is critical for motor control, we currently do not have a consensual definition of proprioception, and also do not have a consensual method to assess proprioception. In neurotypical right-handed individuals, results from an ipsilateral passive matching task consistently revealed that arm proprioception was more precise for the non-dominant elbow and wrist (Abi Chebel et al. 2022, 2023; Oldfield 1971). Recently, we asked neurotypical participants to rate their proprioceptive performance in this task for both arms: right-handers reported higher ratings for the dominant arm, while proprioceptive performance was actually better for the non-dominant arm. We also asked blind participants to rate their proprioceptive performance and right-handers reported higher ratings for the dominant arm, while actual proprioceptive performance was not significantly lateralized.

Using a similar ipsilateral passive matching task, we found proprioceptive deficits for sensory neuropathy patients (Yousif et al. 2015; Miall et al. 2018). However, these deficits were smaller than expected from clinical tests which failed to reveal any tendon reflex and neurophysiological testing which failed to reveal any somatosensory-evoked potential. Overall, such inconsistencies should lead to

a new theoretical, multi-layer model of proprioceptive function (Héroux et al. 2022) which suggests that multiple tests are necessary to assess all aspects of proprioception.

1-E-65 - The influence of tremor on pallidal activity in patients with Parkinson's disease

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<u>Details</u>

Parkinson's disease (PD) is characterized by bradykinesia, rigidity, and resting tremor. Beta activity is known to correlate with bradykinesia while theta oscillations correlated with tremor. Neurons oscillating with the tremor rhythm were observed in the subthalamic nucleus, globus pallidus and ventral thalamus. At the same time properties of non-oscillating pallidal cells in PD with tremor remain unclear.

We analysed single unit activity of 449 cells in the external (GPe) an internal (GPi) segments of globus pallidus in five PD with tremor (PD-Tr) and five without tremor (PD-NoTr) who underwent pallidal deep brain stimulation (DBS) surgery. We separated neurons to tonic, burst and pause pattern using clusterization analysis. Firing rate, coefficient of variance, asymmetry index (median/mean ISI), percent of spikes in bursts and other firing pattern parameters as well as oscillation parameters of single unit activity were analyzed. We also analized randomness (entropy and local variance) of spiking activity.

We found that GPi in PD-Tr characterized by significantly lower firing rate (67 imp/sec in PD-Tr vs. 89 imp/sec in PD-NoTr) and higher irregularity, which is manifested in a high coefficient of variation (1,00 in PD-Tr vs 0,77 in PD-NoTr) and a low asymmetry index (0,68 in PD-Tr vs 0,80 in PD-NoTr). Division of cells into tonic, burst and pause type showed the prevalence of burst and pause cells in GPi of PD-Tr (65%) and tonic cells (60%) in PD-NoTr. Analysis of parameters for each type of cells showed robustly higher spike irregularity and higher randomness and no differences in the firing rate of GPi burst cells. At the same time we found no differences in both distribution and properties of GPe cells. Correlation analysis showed significant (p<0,001) positive relationship between GPi firing rate and irregularity with UPDRS in PD without tremor. At the same time we didn't found any significant correlations in PD with tremor.

We found robust differences in GPi cell activity between PD with and without tremor. We also found strong correlation of pallidal activity with severity of PD in patients without tremor. The results sugest that tremor not only characterized by tremor-related rhythmic activity, but also influence on the pattern of a large percentage of pallidal neurons. The absence of GPe changes may indicate the importance of the "hyperdirect" cortico-STN-GPi pathway in the tremor generation. Further studies of PD with tremor is needed to understand the neuronal mechanism of tremor and it's impact on pallidal activity.

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<u>1-E-66 - Associations between the Neural Mechanisms of Music Listening and Gait in persons with</u> <u>Parkinson's Disease</u>

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<u>Details</u>

The use of music to help persons with Parkinson's disease (PD) move better has been well studied, but the underlying mechanisms remain limited due to limitations in capturing brain activity in clinical settings. Neuroimaging studies have revealed that listening to music activates the ventral tegmental area (VTA). The VTA projects to the dorsal prefrontal cortex (PFC), and previous work in animal models that stimulation of the VTA through results in slow wave Delta band (1-4 Hz) oscillations in the PFC. This suggests that activity in the VTA during music listening may be assessed by measuring activity over the PFC. The purpose of this study is to determine if changes in delta oscillations over the PFC occur with music listening in humans and how they relate to functional movement. Data from four electroencephalographic (EEG) electrodes (AF7, AF8, TP9 and TP10) on a wireless headband were collected at rest and while participants listened to preferred music and white noise. Participants also completed a 15 foot walk immediately after the listening conditions. Power in the Delta band was obtained and normalized to rest for the music and white noise conditions. Gait spatiotemporal data was obtained from Opal wearable sensors. A one way repeated measures ANOVA will be applied. A priori comparisons between listening conditions will also be completed using paired t-tests and effect sizes determined for both EEG and gait outcome measures. Additional analysis to determine if there are associations between the EEG and gait outcomes measures will also be applied. Current results from healthy young adults suggest there may be differences in delta power from electrode AF8 between listening conditions (effect size, d=0.79). Data collections are ongoing and results from persons with PD, healthy older adults, and healthy young adults are expected.

<u>1-E-67 - A robotic object hit and avoid task is sensitive to executive dysfunction in older adults with signs of dementia</u>

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<u>Details</u>

Neuropsychological assessments for dementia include measures of executive control that require sensory and motor processes. While these tasks are meant to be quick, short assessments they fail to capture the role of sensorimotor processes in diminished task performance in aging and dementia. Bimanual rapid motor decision-making tasks like Object Hit (OH) and Object Hit and Avoid (OHA) have shown to be sensitive to cognitive and motor aspects of aging (Watral et al., 2021). However, the impacts of cognitive impairment in older adults in the pre-clinical and clinical stages of Alzheimer's disease on these tasks has yet to be explored. We recruited 67 young adults, 53 healthy older adults and 23 cognitively impaired adults. We defined cognitively impaired as participants who were either diagnosed with early-Alzheimer's disease, diagnosed with mild cognitive impairment, or reportedly healthy individuals that scored poorly on a standard clinical neuropsychological test battery to evaluate cognitive impairment in dementia. Participants completed the OH, OHA and a neuropsychological battery that included multiple

measures of cognitive control, including the Trail Making Test B and the Stroop test. The OH and OHA tasks are administered using the KINARM End-Point device (Kingston, Canada) and require rapid bimanual responses to hit and/or avoid virtual objects. The objects are displayed in the horizontal plane on a display located just above the hands. Each task takes 2 minutes and 30 seconds. During the tasks the objects move towards the participant at a slow speed initially and accelerate as the task progresses. Previous work showed that after controlling for movement speed and sensorimotor processes, older adults exhibited impairments in object processing rate, the proportion of distractors hit, and the number of targets hit, compared to younger adults (Watral & Trewartha, 2021). Importantly, these measures correlated with performance on independent measures of executive control. In the current study, we confirm those results and demonstrate that the same measures are sensitive to cognitive impairment as the cognitively impaired group performed worse than healthy older adults. Those deficits are related to greater executive control deficits in the cognitively impaired group. These findings confirm that rapid motor decision-making tasks like OH and OHA are sensitive to cognitive impairments in the earliest stages of Alzheimer's disease. Future work will seek to better classify different levels of cognitive impairment to provide a framework for diagnosing impairment using the Object Hit and Avoid tasks.

F – Adaptation & Plasticity in Motor Control

<u>1-F-68 - Comparison of implicit motor adaptation between naturalistic and traditional lab-based</u> perturbations

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Details

Over the past several decades, lab-based studies have demonstrated that experiencing an error causes an update to our motor commands. This adaptation is due to the combined output of subconscious and strategy-based learning systems. Theories describing the interaction between these parallel processes are currently derived from highly simplified tasks – commonly a visuomotor rotation (VMR) during brisk movements that primarily involve a single joint. It is unclear to what extent, if any, the learning rules uncovered in these elementary scenarios will generalize to skills we execute in everyday life.

Here we examine motor learning during a naturalistic task using a custom virtual reality program, seeking to understand how our implicit learning system responds to two different perturbation conditions: a VMR and a naturalistic wind, emulating lab-based approaches and real-world conditions, respectively. Forty participants (20/condition) were placed in a virtual environment where they launched a ball towards a visual target. The program was coded in the Unity game engine and run on a Pimax Crystal Head Mounted Display, providing high resolution (35 ppd), frame rate (120 Hz), field of view (115 degree horizontal), and integrated eye tracking. On each trial, participants recharged their launcher, re-aimed, and pushed a button to launch the ball. After a familiarization period, either a VMR or lateral wind was applied to move the ball 30° off-course. Following the adaptation period, feedback was removed and participants were instructed to aim directly at the target, allowing us to measure their implicit aftereffect.

Behavior was more variable than is typically observed in constrained lab conditions, with salient subjectto-subject differences in the primary joints used to re-aim the launcher, and some participants showing aftereffects with a "negative" orientation. Nevertheless, overall, our virtual environment induced subconscious learning (2.2°, one-sample t-test, p=0.002), with similar magnitudes of implicit adaptation between the VMR and wind conditions (two-sample t-test, p=0.76). Closer inspection, however, suggested a puzzling trend: in the VMR condition, individuals with greater total adaptation, exhibited a larger implicit aftereffect (R²=0.40, 3 outliers removed). This is expected in a system where implicit learning is predominantly driven by sensory prediction error: i.e., did the ball's path match my expectations? But in the wind condition, the opposite occurred: greater overall learning predicted less implicit learning (R²=0.32, 3 outliers removed). This behavior is expected in a system where implicit learning is predominantly driven by a performance error: i.e., did the ball hit the target (Albert et al., 2022)?

In sum, our work demonstrates that implicit adaptation occurs in naturalistic learning outside the laboratory but may rely on a different source of error dominated by performance rather than prediction.

1-F-69 - Micro-offline contributions to early skill learning: a comparative analysis

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<u>Details</u>

A remarkable feature of the human brain is the capability of acquiring new skills or knowledge with very little experience (i.e. – one- or few-shot learning). Early learning of challenging sequential motor skills develops rapidly over only a few minutes with performance gains predominantly emerging following short, interleaved rest (micro-offline gains) rather than during practice. A major challenge of investigating skill learning dynamics through behavioral performance measures is that the performance at any point in time is the mixed result of both facilitatory (e.g. – improved performance due to learning) and inhibitory (e.g. – fatigue) influences. The original investigation of micro-offline learning [1] mindfully incorporated crucial recommendations from prior work [2] intended to maximize learning-related effects and minimize inhibitory ones. This included (a) utilizing 10s practice trials and (b) constraining early learning analyses to the "early learning" period where 95% of skill gains occur and prior to the emergence of strong within-trial performance drops (i.e. – micro-online drops) attributed to reactive inhibition.

Retroactive interference introduced immediately after each practice period significantly reduces microoffline gains indicating stabilization of the motor memory at a scale of seconds [3], which is consistent with a form of rapid consolidation. Furthermore, supporting this interpretation, hippocampo-neocortical neural replay (measured with MEG) and hippocampus ripple (known markers of neural replay measured directly with invasive micro-electrodes) density during inter-practice rest intervals explain micro-offline gains and total early learning in humans. In spite of this evidence to the contrary, recent work posed that micro-offline gains instead express recovery from motor fatigue [4] or do not reflect offline learning at all [5]. To better understand the drivers of these interpretation differences, we performed a comparative analysis on data acquired for the same sequence skill (i.e. – 4-1-3-2-4) from multiple research groups where practice (from 5 to 30s) and rest (from 10 to 60s) durations varied [3, 4]. Importantly, we applied the same analysis constraints utilized in our original investigation [1] to all datasets.

This comparative analysis revealed that early learning was predominantly explained by micro-offline gains in all groups despite variations in practice and rest duration. We found that conflicting interpretations were largely driven by the discarding of the initial "warm-up" practice trial or sequence [4] or the inclusion of pre-intervention "test" data in the design, both of which truncated total learning

by up to 20% [4, 5]. Crucially, performance differences related to the specific combination of rest and practice intervals largely emerged after early learning and performance had plateaued [1, 4].

We conclude that micro-offline gains consistently explain early learning dynamics across all of the considered datasets [3, 4]. As defined, early learning cannot be accurately tested if practice trials are arbitrarily excluded (i.e., warm-up [4], test [5]) or compared to non-learning settings (non-repeating sequences) [5].

References

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1-F-70 - Sensorimotor co-adaptation during reaching in a visuomotor rotation task

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<u>Details</u>

From a parent guiding their toddler when learning to brush their teeth to robot-guided neurorehabilitation, humans have a remarkable ability to seamlessly interact and adapt alongside other humans and synthetic agents. Previous work has shown that adaptive agent algorithms and devices that interact with humans can lead to greater movement accuracy and energy efficiency. Yet, the mechanisms of co-adaptation that govern these seamless sensorimotor interactions remains unclear. Sensorimotor adaptation in a single individual involves multiple timescales that involve both slow motor processes and fast cognitive processes, which has been accurately captured using a two-state model. Here, we built upon this state-space approach to investigate co-adaptation of human-agent pairs in a visuomotor rotation task. Across two experiments, human participants grasped the handle of a Kinarm Endpoint Lab and made reaching movements to a virtually displayed target. In Experiment 1, participants completed 50 baseline trials followed by 200 adaptation trials. During baseline trials, all participants performed alone and received veridical cursor feedback at the end of each trial. During rotation (30-deg) trials, participants performed their reaches with either a fast-agent or a slow-agent partner based on the fast and slow states of the two-state model (Smith et al. 2006). Cursor feedback representing the joint contributions of the human-agent pair was provided at the end of each trial. In Experiment 2, all participants completed two sessions that consisted of 50 baseline trials, 200 adaptation trials, 20 counter-adaptation trials, and 50 error clamp trials. In session one, all participants performed the baseline and error clamp trials alone. During the adaptation and counter-adaptation trials, participants performed their reaches with a fast-agent partner, a slow-agent partner, alone with the full rotation (30-deg), or alone with half the rotation (15-deg). Session one and two were separated with a 5-min break to examine savings, where previous adaptation to a visuomotor rotation leads to faster re-adaptation. All participants performed session two alone. In Experiment 1, participants paired with the fast-agent contributed less to correcting the reach error early in adaptation trials, but were responsible for most of the correction in late adaptation trials. In contrast, participants paired with the

slow-agent corrected for a larger proportion of the early error, but their contribution tended to drift over trials. In Experiment 2, session one results were consistent with Experiment 1. Interestingly, the participants paired with the slow-agent partner showed greater savings when performing alone in the second session compared to those paired with the fast-agent partner. Overall, our results suggest that the the learning and retention rates of an adaptive agent strongly influences the equilibrium of overall and individual performance during co-adaptation.

<u>1-F-71 - Reshaping circuit electrophysiological properties via noninvasive stimulation: short-term</u> <u>plasticity in humans</u>

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Details

Non-invasive spinal stimulation has emerged as a promising neuromodulatory approach to modulate spinal excitability. This study investigated the effects of sub-motor threshold, grid-patterned transcutaneous spinal cord stimulation (tSCS) applied over the lumbar spinal cord in neurologically intact individuals. The primary objective was to evaluate tSCS-induced modulation of polysynaptic reflex pathways involving motoneurons and interneurons, likely recruited via $A\beta/\delta$ fiber-mediated cutaneous afferents.

Stimulation was delivered using two grid electrode configurations designed to generate net electric fields oriented transversely or diagonally to the spinal axis, with the grid center aligned over the T10-T11 spinous processes. Participants received 20 minutes of stimulation while seated. Reflex circuit excitability was assessed 30 minutes post-stimulation, focusing on the tibialis anterior flexion reflex and the soleus H-reflex to differentiate tSCS effects on polysynaptic and monosynaptic pathways and examine the spatial influence of grid stimulation.

The results demonstrated that tSCS induced significant inhibition of the flexion reflex, regardless of montage, with the diagonal grid configuration producing a more pronounced suppression of reflex duration compared to the transverse montage. These findings suggest that grid-patterned tSCS can selectively modulate polysynaptic spinal circuits, offering montage-dependent control over spinal excitability and highlighting its potential as a targeted neuromodulatory intervention.

1-F-72 - Disruption of dorsal premotor cortex impairs retention of human motor learning

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<u>Details</u>

Recent studies have questioned the role of the primary motor cortex (M1) in the encoding of motor memories, instead proposing a critical contribution from the postcentral cortex. Evidence indicate that disruption of posterior postcentral gyrus following visuomotor training significantly impairs motor retention, whereas disruption of M1 does not produce any impairment, suggesting a minimal involvement of primary motor regions in this process (Ebrahimi & Ostry, 2024; Ebrahimi et al., 2024). Nevertheless, a recent functional magnetic resonance imaging study has identified substantial learning-

related changes within the dorsal premotor cortex (PMd) during motor sequence acquisition, though the precise function of PMd in retention remains unclear. In the present study, we tested the hypothesis that newly learned movements involve learning related updates to PMd. Participants were trained using a visuomotor adaptation paradigm involving a gradual 30-deg rotation of visual feedback. Continuous Theta Burst Stimulation (cTBS) was applied following training to specific cortical regions and retention was assessed 24h later. Targeted stimulation was applied to the primary motor cortex (M1) and the dorsal premotor cortex (PMd), with the occipital cortex serving as a control site. Retention was evaluated using active movements with no visual feedback whatsoever. The results demonstrated that cTBS-induced suppression of M1 had negligible effects, with retention performance remaining comparable to that of the control condition. These findings suggest that the dorsal premotor cortex, alongside the postcentral cortex (Ebrahimi & Ostry, 2024; Ebrahimi et al., 2024), constitutes an integral component of the neural network underpinning the retention of newly acquired motor skills. Conversely, the primary motor cortex appears to play a limited role in this process.

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1-F-73 - Integration of touch location with body posture for an additional robotic body part

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Details

Having an extra body part could expand our movement abilities, allowing us to perform complex manual tasks and develop novel movements. However, it is unclear how well we can incorporate additional limbs into our brain's body representation, allowing us to use them in a natural, fluent manner. A key question is whether we can develop a multisensory body representation for an additional robotic body part, allowing us to predict its movements and sensory interactions with objects. Multisensory integration of touch location with body posture is crucial for us to be able to make movements towards our own body, as we must combine touch location on the limb with the limb posture to be able to derive a spatial movement target. In this study, we explored whether participants can integrate touch location and body posture for an additional robotic thumb, The Third Thumb (Dani Clode Design). We developed a novel marked-based motion tracking setup to record participants' pointing movements to touch stimuli at four positions along the Third Thumb. In each trial, participants felt a touch stimulation from one of four vibration motors on the Third Thumb. They then used intrinsic touch sensation information, i.e. the touch sensations arriving at the connection of the Third Thumb with the side of their hand, to make a pointing movement with their left index finger to the location on the Third Thumb that they judged as the origin of the touch stimulus. Participants' vision was occluded during each trial. Across the session, the Third Thumb was positioned in six different postures. The Third Thumb and participants' index finger pointing movements were tracked using Apriltag markers detected via a

stereocamera. Our preliminary results show that participants could distinguish between different touch locations along the Third Thumb, demonstrating that participants can utilise differences in intrinsic touch sensations to determine touch location. This ability has been previously shown for handheld tools. We next explored whether participants showed any differences in behavioural performance across different Third Thumb postures and touch locations along the Third Thumb by measuring the angle and distance between the pointing vector defined by the participants' pointing (index) finger and the touched location on the Third Thumb. Both measurements identified a significant effect of touch location, driven by worse pointing performance to touched locations at the tip of the Third Thumb, compared to other locations along the Third Thumb. We did not identify any performance differences driven by posture. Our results demonstrate that participants can determine touch location in 3D space. Our future research will explore whether this ability is strengthened following intensive Third Thumb.

1-F-74 - How do humans manage the curse of dimensionality in motor learning?

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<u>Details</u>

The human ability to control complex movements with multiple degrees of freedom presents a fundamental paradox in motor learning. While humans readily perform multi-dimensional movements, the "curse of dimensionality" suggests that learning should become exponentially more difficult as dimensions increase, potentially making such control intractable. How, then, do humans manage to learn and control movements with multiple dimensions?

To address this question, we developed a novel online sensorimotor task where participants (n=75) used keyboard inputs to align one to four independently controllable circles to center positions, framed as a time-based lock-picking challenge. Participants were divided into five groups that differed during the learning phase (control with no learning phase, 1D, 2D, 3D, and 4D learning phase). Performance was measured as the time to align all circles. We assessed both learning progression by comparing learning curves between groups during the training phase and generalization through testing performance on all possible circle position configurations (both trained and untrained) before and after the learning phase.

Analysis of the (logarithmic) learning curves revealed approximately an additive shift with increased dimensions, indicating an exponential increase in time to learn the skill and limited transfer of learning across control elements. This limited generalization was further confirmed by posttest performance in untrained circle positions. Notably, participants predominantly adopted sequential control strategies, with significant individual variation. While some participants manipulated only one dimension at a time, others coordinated two simultaneous dimensions, and very few attempted to control three or more. This preference for sequential control changed only slowly and persisted even after four days of training.

Although sequential control of individual elements allows for faster short-term task completion, this strategy may ultimately limit learning in the long term. The poor generalization we observed suggests that breaking down multi-dimensional control into sequences leads to suboptimal performance compared to what might be achieved through integrated control strategies. Thus, our findings suggest that humans primarily cope with the curse of dimensionality through sequencing rather than developing unified control solutions, highlighting fundamental constraints in learning high-dimensional motor tasks.

1-F-75 - Type and timing of error signals on initial implicit changes in visuomotor adaptation

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<u>Details</u>

While implicit visuomotor adaptation has been widely studied, most research has focused on cumulative learning over multiple trials, leaving the earliest stages of adaptation—particularly the role of different error signals and their timing in single-trial learning—poorly understood. Current models suggest that error magnitude and attribution influence adaptation, yet their specific impact on the initial implicit response remains unclear.

To address this gap, we conducted a series of studies to precisely quantify the initial implicit changes that occur during classic, movement-contingent adaptation in response to altered visual feedback of the hand. We systematically examined how different types of error signals and their timing influence this early stage of implicit adaptation. Using a single-trial learning approach, we assessed these effects across varying perturbation magnitudes to isolate the specific contributions of error processing to visuomotor recalibration.

Our findings indicate that the initial implicit change in reach direction after a single reach with a misaligned cursor remains fairly stable across perturbation sizes. Deviations averaged about 3.6 degrees for smaller perturbations of 5 and 10 degrees, while for perturbations from 15 to 90 degrees, deviations were closer to 6 degrees. This suggests that error magnitude does not reduce the implicit contribution to adaptation, as proposed by models of error attribution. Instead, the initial change in reach aftereffects appears to be "capped," similar to findings on learning extent limits.

Furthermore, when we removed task or performance errors by having participants reach to wide arcshaped targets—ensuring that even misaligned cursor landed within the target—we still observed significant reach aftereffects of approximately 4 degrees for these larger visuomotor rotations. This suggests that while sensory prediction errors are the primary driver of implicit adaptation, task errors also play a contributing role to these initial changes in reach direction.

Lastly, when feedback of the misaligned cursor was limited to the end of the movement—i.e., terminal or endpoint error—the single-trial aftereffects were substantially reduced, averaging around 2 degrees in the expected direction. However, despite this reduction, the deviation remained significant in the direction of learning across different rotation magnitudes. Notably, increasing the delay between movement offset and endpoint feedback to 0.2, 0.4, 0.8, or 1.6 seconds did not eliminate this small but persistent aftereffect, suggesting that implicit adaptation can still occur, albeit at a reduced magnitude, even when terminal error information is delayed.

1-F-76 - The influence of leg movements on performance during a visuomotor reach adaptation task

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<u>Details</u>

Cerebellar patients exhibit reduced learning in visuomotor reach adaptation paradigms involving errorclamp manipulations, in which participants are instructed not to try to control the movement of a cursor shown moving at an angle relative to the intended movement, suggesting that the implicit learning observed in this task is cerebellar-dependent (Morehead et al., 2017). Delay eyeblink conditioning is another cerebellar-dependent task, and studies using this model have influenced theories of error-based cerebellar learning (see Raymond & Medina, 2018 for review). If cerebellar-dependent learning involves a shared set of circuit elements and underlying principles (Schmahmann, 2000; but see Cerminara et al., 2015, Diedrichsen et al., 2019), it may be that manipulations that affect eyeblink conditioning also influence reach adaptation. Work in a mouse model has shown that head-fixed treadmill running enhances delay eyeblink conditioning by reducing the threshold for activation of mossy fibers thought to encode information about task context (Albergaria et al., 2018). Here, we set out to test whether taskirrelevant movements influence learning in reach adaptation in a similar fashion, predicting that ongoing movements should enhance adaptation or serve as a contextual cue affecting the expression of learning. To this end, human participants (n = 48) performed a center-out reaching task in which they observed a 30° error-clamp during their movements. Half of the participants pedaled on an underdesk elliptical during training, and the other half held their legs stationary. After training, half of the participants either started or stopped pedaling during a final block of reaches, to allow us to evaluate whether pedaling affected the generalization of learning. Although pedaling did not affect the degree of reach adaptation during any phase of the experiment, pedaling affected participants' ability to find the center of the workspace between trials during the generalization block. During this period, participants who trained without pedaling exhibited a deficit when returning to the center of the workspace upon the initiation of pedaling, while participants who pedaled during the task exhibited no such deficit when keeping the legs stationary. These data suggest that participants who pedaled during the task learned to coordinate movements across multiple body parts in a way that participants who were stationary during the task, or that participants who pedaled during the task learned to parse proprioceptive information from the hand and arm from sensory "noise" coming from the legs. The data also suggest that categorical changes in ongoing, task-irrelevant movements are not sufficient to influence the degree of implicit reach adaptation acquired or expressed in humans.

1-F-77 - Whole body motor adaptation in goldfish using fish operated vehicle

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<u>Details</u>

Motor adaptation is crucial for animals navigating diverse environments, and we don't understand how this process works in fish especially when compared to mammals. This prevents a comprehensive view of adaptive motor control across vertebrates. Here we show that goldfish operating a Fish Operated Vehicle (FOV) adapt swimming behavior to achieve targets when vehicle movement is perturbed by a rotational transformation. Goldfish gradually adjusted their swimming patterns to compensate for the perturbation and had aftereffects when the perturbation was removed. Fish showed improved performance when the perturbation was re-introduced, although their initial learning rate in the second exposure was slower compared to the first exposure. These findings reveal that while goldfish can adapt to novel dynamics, their adaptation mechanisms may differ from those of mammals. This study broadens our understanding of motor adaptation across species, contributing to a more comprehensive view of motor learning in vertebrates.

1-F-78 - Motor adaptation via pure visual change

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Details

Beyond having visual feedback of movements be well-timed, what are the minimal sorts of visual signals that are sufficient for visuomotor adaptation? In typical visuomotor rotation (VMR) adaptation tasks, the relevant visual feedback involves objects defined by some particular features that can be perceived via segmentation from the background — such as a white disc on a black screen that either serves as a visual cursor moving with the hand (continuous feedback), or blinks into existence at some point during the movement (endpoint feedback). As long as this kind of familiar feedback is not delayed relative to movement onset, perturbing it will lead to adaptation. But is segmentation of an object from the background truly required? Might it be possible to drive visuomotor adaptation even in featureless displays — in which it is never possible to segment an object from the background — and in which there are no enduring properties from moment to moment? To find out, we explored visuomotor adaptation with "featureless objects". In experiment 1, subjects performed a VMR task with a novel form of feedback – pure color change. The task workspace was tiled with blue squares, with the initial contrast intensity (i.e., the shade of blue) differing randomly across the squares on every trial. When subjects moved in this workspace, visual feedback of their hand position was signaled only by changing each new square they moved into from one random shade to a different random shade. As a result, it was never possible to see the current location in any static frame, and no particular shade persisted from moment to moment during movement. This feedback could be rotated, such that a movement trajectory through the workspace would cause a sequence of random color changes along a line of squares offset from the reach trajectory. Subjects reached to targets (red squares) under baseline and rotated conditions. An aftereffect phase was used to measure the degree of final implicit adaptation. Subjects were able to counteract the rotation during the learning phase. Critically, implicit aftereffects were significant. Thus, pure color change that is spatiotemporally correlated with movement can signal an error and induce motor adaptation. Next, we extended this result to more abstract visual changes. In experiment 2, the reaching workspace consisted of a ring of black crosses, each with a random orientation on every trial. When people moved beyond the radius of the workspace, a single cross changed orientation by rotating 45 degrees in a random (CW or CCW) direction, constituting a "featureless" form of endpoint feedback. The task required subjects to try to get a blue cross (the target) to change orientation on each trial. As in experiment 1, subjects performed a baseline phase with no rotation, a rotation learning phase, and an aftereffect phase. Subjects again learned to counteract the rotation and showed significant aftereffects. Taken together, these results suggest that error-based motor learning is sensitive to surprisingly abstract visual consequences of motor commands – pure visual change that is spatiotemporally correlated with movement, even without visual features that can be segmented from the background or that persist over time.

<u>1-F-79 - Transcranial ultrasound stimulation (TUS) of the hippocampus affects rapid motor memory</u> <u>consolidation</u>

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Details

Recent evidence indicates that performance improvements observed during the acquisition of a new motor sequence occur predominantly during quiet rest periods interspersed with practice sessions

(micro-offline gains, MOGs). However, it remains uncertain whether these MOGs are primarily attributed to the hippocampus or other cortical regions involved in motor skill learning. This study establishes that the hippocampus plays an essential role in MOGs, and its disruption enhances initial motor performance while expediting stabilization.

In this study, young adult participants utilized their non-dominant hand to perform a 5-item explicit sequence (4-1-3-2-4) tapping task designed to assess motor skill learning across acquisition and test phases. Transcranial ultrasound stimulation (TUS) was applied contralaterally to the non-dominant hemisphere hippocampus prior to the acquisition phase to transiently downregulate hippocampal activity. The practice phase of the sequence tapping task comprised 36 alternating 10-second practice and rest intervals, whereas the test phase included 9 trials conducted 24 hours later. Performance metrics included speed, defined as the time interval in seconds between correct keypress transitions, and accuracy, defined as a correct keypress. Micro-online gains were measured as the difference in speed between the last 5 correct transitions of a block and the first 5 correct transitions of a block.

Results indicated differences between the control group and the experimental group across the overall performance curve. In terms of microscale learning, the experimental group demonstrated contributions from both micro-online and micro-offline gains to total learning, whereas the control group's total learning was primarily attributed to micro-offline gains.

The findings reveal that hippocampal downregulation significantly reduced MOGs during early learning while leading to higher initial performance levels and a faster acquisition plateau. These results highlight the dynamic role of the hippocampus in mediating both performance and learning stability during motor skill acquisition, providing valuable insights into memory-motor integration.

1-F-80 - Learning sign language with real-time kinematic feedback

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<u>Details</u>

Mastering sign language demands an extraordinary level of motor dexterity. Each gesture must be executed with precision, speed, and seamless coordination between the hands, fingers. Investigating how sign language is acquired can therefore provide a window into how humans learn to select and execute complex, dexterous movements of the hand.

Despite the complex motor demands of signing, traditional instruction offers little real-time kinematic feedback to refine movements. Instead, learners receive delayed and imprecise verbal corrections—a form of feedback that may hinder motor skill acquisition. Moreover, no study has systematically measured how hard it is to learn different signs, let alone why. Is a sign easier to learn because it looks like what it means (iconicity), because it is biomechanically simpler, or because of some interplay between the two? Answering this question could help optimize sign language curricula, making sign language learning faster and more efficient.

To overcome these limitations, we developed GestureQuest, a fun sign language learning tool that leverages markerless tracking and a machine-learning-based sign recognition system to deliver continuous kinematic feedback. This technological advance not only allows learners to refine their movements with precision but also allows us to rigorously quantify hand kinematics in real-time. With

GestureQuest, novice signers attempted to learn all 26 ASL alphabet signs, allowing us to track learning across a rich set of gestures while minimizing the influence of prior semantic knowledge on learning. Novice signers first performed the signs without feedback (baseline), then trained with continuous kinematic feedback, and finally demonstrated retention in a post-training phase without feedback.

Novices made striking gains in both the accuracy and speed of ASL letter production. In just 45 minutes, they quadrupled their repertoire—starting from an average of 4 correct signs to 16. These rapid improvements hint at the beneficial effects of continuous kinematic feedback and gamification in accelerating sign language learning. Moreover, contrary to prior studies, iconicity did not predict the ease or difficulty of sign production. Instead, our findings highlight biomechanical complexity and letter frequency in English as key factors in determining sign complexity, making letters like Q and X more difficult to produce than A or B.

Together, these preliminary findings provide new insight into how people acquire dexterous hand movements and pave the way for an evidence-based approach to sign language instruction.

<u>1-F-81 - A theoretical model of acquisition and long-term retention in multifrequency bimanual</u> <u>coordination</u>

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<u>Details</u>

Learning a novel motor skill requires multiple neural processes over multiple time scales. Strides have been made in modeling how humans improve accuracy through repetition or adapt sensorimotor skills to perturbed environments. However, the changes in the kinematic characteristics across practice have not been thoroughly incorporated into a computational model. From a dynamical systems perspective, bimanual coordination is a paradigmatic problem in rhythmic movement coordination, which has received extensive attention in both experimental and modeling studies. The classic Haken-Kelso-Bunz model for coordination in a 1:1 frequency ratio has been extended to multifrequency (non-1:1) coordination as well as to learning of 1:1 coordination at a specified relative phase. To date, however, it remains difficult to model the process of learning multifrequency bimanual coordination, partly due to the mathematical complexity of the nonlinear oscillator models previously used. Here, we present a simple mathematical model derived from weakly connected neural networks, the canonical model, and show that the model can replicate the multi-timescale learning process observed in a previous study on 3:1 coordination in dual hand-held pendulum swinging.

The model consists of two self-sustained, adaptive-frequency oscillators coupled via plastic connections that evolve according to Hebbian learning rules. In the canonical model, different modes of coordination (e.g., 1:1 and 3:1 coordination) are supported by distinct coupling terms, which enables the model to learn and forget individual modes of coordination separately. We first analyze the model dynamics by examining the contribution of each model component to the overall dynamics. We then replicate the previous empirical data by simulating the experimental procedures for practice and long-term retention of 3:1 pendulum swinging. We show that the multiple timescales of learning observed for task-specific variables can be modeled by distinct time constants for frequency adaptation and Hebbian learning. Notably, the experimentally observed differences in learning rates between the time and frequency domains are reproduced in the canonical model. Furthermore, the model successfully replicates the timescales of forgetting during retention. We also show that individual differences in the acquired 3:1

relative phase, a variable not specified by the task, can be explained by the nature of oscillatory Hebbian plasticity in the absence of forced phase relationship.

Taken together, the present study demonstrates the advantages of the canonical model over more complex nonlinear oscillator models that have been used to model bimanual coordination, such as the van der Pol-Rayleigh oscillator. The canonical model allows us to model the multi-timescale process of acquiring multifrequency coordination and the learning and forgetting of individual modes as the strengthening and weakening of coupling coefficients.

1-F-82 - Sensorimotor and neurophysiological underpinnings of speech audio-motor memories

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<u>Details</u>

Our knowledge of human sensorimotor learning and memory is predominantly based on limb movements and the visuo-spatial workspace. Humans also have a remarkable ability to produce and perceive speech sounds. We asked if the human speech-auditory system could serve as a model to probe sensorimotor memory in a workspace which is functionally independent of the visuo-spatial one. Using adaptation to real-time, altered auditory feedback of the first formant frequency (F1) of a vowel, we sought to determine whether speech motor adaptation leads to a formation of a new vowel versus adjustments toward well-learned existing vowels in English vowel space. The first two formant frequencies (F1 and F2) that characterize the vowel space were used to determine the positions of unperturbed vowels ("dep", "dap", and "dip" during baseline), along with that of the perturbed vowel ("dep" during the end of learning). We observed that speech production of "dep" following learning shifted considerably relative to the location of "dep" at baseline in the vowel space (n=14). This shift did not overlap with the neighboring well-learned English vowels, but rather stabilized where no English vowel exists, establishing that speech motor adaptation can indeed facilitate production of a new vowel versus a mere shift towards existing neighboring vowels. Next, we investigated the durability of the speech motor memory (8- and 24-hour delay), and its sensitivity to the manner of acquisition (abrupt versus gradual perturbation). We observed extensive retention of learning (~70%) and an insensitivity of this memory to the manner of its acquisition (n=58 across four conditions). Notably, this memory was accessible in presence of either speech or noise feedback immediately after learning, but when tested 8 or 24 hours later, memory retrieval was negligible in presence of noise feedback, yet considerable after reintroducing speech feedback. These findings support the notion that by contextualizing memories, the brain can simultaneously store multiple modes of speech production (Rao and Ostry, under review). In the third and an ongoing study, we investigate the neural substrates that causally contribute to the speech motor memory retention. With neuroimaging evidence suggesting sensitivity of superior temporal gyrus (STG) to vowel characteristics, we deliver continuous theta burst transcranial magnetic stimulation (cTBS) over the left or right STG immediately following speech motor adaptation, and test retention ~24 hours later. The control conditions include either no stimulation or cTBS over a neutral site (ongoing). Current trends indicate reduced retention following disruption to STG on either hemisphere versus control, suggesting causal involvement of bilateral STG in speech motor memory retention (n=40 currently). In summary, our series of experiments present evidence of new vowel production following speech motor adaptation, extensive speech memory retention, its insensitivity to the manner of memory acquisition, the time-dependence of memory retrieval on the contextual availability of speech feedback, and causal involvement of bilateral STG in memory retention.

Collectively, the findings establish speech audio-motor system as a behaviorally relevant but functionally independent workspace from its visuo-spatial counterpart to probe sensorimotor learning and memory.

<u>1-F-83 - Investigation of sensorimotor interactions between the trunk and the upper limb in healthy</u> volunteers

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Details

Referred sensation (RS), described as the sensation evoked by stimulating the skin surface in a place other than the stimulated region, is commonly reported following severe peripheral injuries. Our team has documented the emergence of RS over the rib cage after stimulation of the forearm skin in patients with brachial plexus injury (BPI) who have undergone biceps reinnervation using the intercostal nerve (ICN).

Afferent inhibition (AI) consists in modulating the excitability of the primary motor cortex (M1) by electrical stimulation of sensory afferents. Recent research indicates that AI exhibits a somatotopic organization but may also reveal broader inhibitory circuits, such as interactions between the face and the hand.

This study aims to investigate sensorimotor modulation between the trunk and the upper limb in healthy volunteers and in BPI patients. Afferent inhibition patterns of the biceps muscle were analyzed following peripheral electrical stimulation of the cutaneous territories of the musculocutaneous (MC), ulnar, and intercostal nerves. Initially, transcranial magnetic stimulation (TMS) was utilized to map the representation of the biceps in M1. Subsequently, sensory thresholds for the electrical stimulation were determined for the forearm, little finger, and thoracic regions.

For the AI protocol, peripheral electrical stimulation was applied at an intensity of three times the sensory threshold and TMS was delivered to the biceps hotspot with the pulse intensity calibrated to induce an average muscle response with a peak-to-peak amplitude of 0.5 mV. The time intervals between peripheral electrical stimulation and the TMS pulse were 15, 20, 25, 30, 35, 40 and 45 ms.

Fourteen healthy volunteers have been evaluated. In two of these subjects, it was not possible to identify a hotspot that evoked responses in the biceps. Of the 12 subjects who had biceps-evoked responses, two did not complete the AI protocol. Therefore, data analysis was based on a total of 10 volunteers.

The hand-biceps protocol revealed an inhibition peaked at 45 ms (13.41%). The forearm-biceps protocol demonstrated an inhibition occurring at 25 ms (3.33%). As for the chest-biceps protocol, inhibition was observed across intervals from 15 to 35 ms, with the highest rates in 20 and 30 ms (5.23 and 5.12%, respectively).

In conclusion, preliminary results indicate a inhibition upon the biceps muscle after stimulating the hand, the forearm and chest regions in control subjects. As the intercostal grid and the biceps are physiologically connected in BPI patients undergoing ICN to MCN transfer surgery, stimulating both the skin region innervated by the MCN and that innervated by the ICNs would result in inhibition of biceps MEPs.

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1-F-84 - Contributions of visual, dynamic, and kinematic cues to compositional motor learning

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<u>Details</u>

Understanding how the brain forms compositional representations is a key challenge in neuroscience. Compositionality allows the motor system to integrate learned components, supporting flexible adaptation to new conditions. While extensively studied in cognitive domains (Austerweil & Griffiths, 2013; Lake et al., 2017), its role in motor learning remains unclear. Prior work (Flanagan et al., 1999; Davidson & Wolpert, 2004) suggests compositional motor representations, but the conditions driving their emergence are unknown. Here, we examine how visual, dynamic, and kinematic cues contribute to compositional motor learning.

Visual and Dynamic Compositionality

Using a 3BOT robotic interface and VR headset, participants made reaching movements while experiencing one of six different velocity-dependent force fields cued by distinct control points (visual cues; Heald et al. 2018). We trained participants on two elemental visuo-dynamic objects (distinct control points and fields) and four probe objects in a pseudorandom order. The probe objects were: (i) only visually compositional (both control points presented simultaneously but novel field), (ii) only dynamically compositional (the sum of elemental fields but not their visual counterparts), (iii) both visually and dynamically compositional, or (iv) neither visually nor dynamically compositional (effectively another element). During a test phase, the gain of an elemental force field was manipulated, and we examined adaptation changes for the probe objects (channel trials only). Only probe objects with dynamic compositional cues exhibited modulation, indicating partial compositional representations. Visual compositionality alone did not produce modulation, implying independent representations in the absence of dynamic compositional cues.

Kinematic and Dynamic Compositionality

In a follow-up experiment, visual cues were replaced with lead-in and follow-through movements as kinematic compositional cues. For kinematically compositional trajectories, both the lead-in and follow-through movements of the constituent elemental trajectories were combined. Using the same structure as the first experiment, kinematic compositional cues were found to produce partial compositional representations alongside dynamic cues. Additionally, combining kinematic and dynamic cues resulted in stronger compositional modulation than either cue alone, suggesting the motor system integrates compositional information across multiple cues.

Conclusion:

Our findings reveal that compositional representations emerge from dynamic (force fields) and kinematic (lead-in/follow-through) cues. While both visual (control points) and kinematic cues support learning multiple force fields, only kinematic cues yield compositional memories, highlighting the unique contribution of kinematic cues in compositional motor learning.

1-F-85 - Motor unit mechanisms of speed control in mouse locomotion

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Details

During locomotion, the coordinated activity of dozens of muscles shapes the kinematic features of each stride, including systematic changes in limb movement across walking speed. Motor units, each of which consists of a single motor neuron and the muscle fibers it innervates, contribute to the total activation of each muscle through their recruitment and firing rate when active. However, it remains unknown how the nervous system controls locomotor speed by changing the firing of individual motor units. To address this, we combined quantitative behavioral analysis of mouse locomotion with single motor unit recordings from the lateral and long heads of the triceps brachii, which drive monoarticular extension of the elbow and biarticular movements of the elbow and shoulder, respectively. In contrast to prior studies employing bulk EMG to examine muscle activity, our recordings revealed the diversity of spike patterning across motor units as well as systematic differences in motor unit activity across muscles and locomotor speeds. First, motor unit activity differed significantly across the lateral and long heads, suggesting differential control of these two closely apposed elbow extensor muscles. Second, we found that individual units were recruited probabilistically during only a subset of strides, showing that bulk EMG signals consistently present in every stride in fact reflect stochastically varying subsets of individual motor units. Finally, although recruitment probability and firing rate both increased at faster walking speeds, increases in recruitment were proportionally larger than rate changes, and recruitment of individual units accompanied changes in limb kinematics. Together, these results reveal how the firing of individual motor units varies systematically across muscles and walking speeds to produce flexible locomotor behavior.

1-F-86 - Neural mechanisms of implicit and explicit motor learning

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<u>Details</u>

Motor learning—the process of refining movements through feedback and practice—is traditionally described as an implicit, non-declarative process. This assumption has shaped dominant neuroanatomical frameworks of motor learning.

However, these frameworks rest on uncertain neuropsychological foundations. First, they rely on underpowered lesion studies, limiting clear structure-function inferences. More critically, mounting evidence highlights the essential role of explicit strategies in motor learning, rendering any framework that ignores strategic contributions incomplete.

To address these limitations, we present a revised neuroanatomical framework integrating implicit and explicit processes in motor learning. Grounded in a meta-analysis spanning five decades, our synthesis incorporates data from over 2,000 patients and controls with lesions affecting peripheral (visual and proprioceptive), subcortical (cerebellum, basal ganglia, hippocampus), and cortical (parietal, frontal) regions. We further integrate findings from novel learning assays designed to dissociate implicit and explicit contributions. Altogether, our revised neuroanatomical framework provides a clearer and more comprehensive account of the neural mechanisms that support multiple processes underlying motor learning.

1-F-87 - Modulations of the implicit recalibration system during De Novo motor learning

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Details

Implicit adaptation is a fundamental process in sensorimotor adaptation, operating automatically to calibrate the sensorimotor map based on sensory prediction errors. Traditionally, this system is considered rigid, unable to adjust to specific task demands. For example, implicit adaptation operates in a fixed direction, effectively compensating for rotational perturbations. However, many studies have shown that for mirror reversal tasks, implicit adaptation operates in a "wrong" direction, which amplifies the error rather than reducing it. In such cases, a distinct learning process known as de novo learning is required to acquire new mappings.

While implicit adaptation is not initially useful for learning mirror reversal, we explored whether the implicit system could be modulated after participants had acquired a new mapping. In Experiment 1, participants underwent a month of mirror reversal training, engaging daily in center-out reaching, point-to-point reaching, and continuous tracing tasks. Intriguingly, we found that the direction of implicit adaptation, initially counterproductive, eventually reversed and corrected for errors in the mirror direction. This suggests that the implicit adaptation system can adapt within a newly acquired map. Furthermore, when participants alternated between mirror and standard maps across trials, they demonstrated the ability to adapt in opposite directions simultaneously, indicating separate implicit memories for the same target or reaching directions across different maps.

To identify the critical task components that facilitate this reversal in implicit adaptation, we compared the effects of different training tasks in Experiment 2. Participants were trained exclusively in either center-out reaching or continuous tracing. The results showed that the center-out reaching group exhibited a faster reversal in implicit adaptation, indicating that feed-forward learning alone is sufficient for this reversal and that feedback control is not necessary.

Finally, we modeled these findings using a two-layer neural network representing the cerebellum and cortex. We trained the cerebellar layer in a standard context to compensate for rotational errors, then fixed this layer while training the cortical layer to learn mirror reversal. After this, we induced small perturbations atop the mirror reversal context. The network produced outputs that correctly compensated for errors, suggesting that modifications within the cortical layer alone are sufficient to reverse implicit adaptation, without the need to modulate the cerebellar implicit system during de novo learning.

1-F-88 - Motor decision is optimally tuned by the uncertainty in the environment and the body

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Details

Human motor behavior is remarkably adaptable, enabling rapid adjustment to environmental uncertainty. In this study, we examined how different sources of uncertainty—environmental volatility, environmental stochasticity, and internal motor noise—influence action selection and learning during a dynamic motor task. Participants engaged in a virtual air hockey game where they controlled a paddle

via a trackpad to strike a puck toward a goal. The puck's trajectory was influenced by an externally applied wind, whose properties were systematically manipulated. Environmental uncertainty was varied along two dimensions: volatility, defined as the rate and magnitude of changes in wind direction and strength, and stochasticity, defined as random fluctuations in wind strength implemented via Gaussian noise.

In Exp 1, participants were randomly assigned to one of four groups in a 2×2 design that crossed high versus low volatility with high versus low stochasticity. Participants initially exhibited increased errors immediately following a change in wind conditions, followed by a rapid reduction in error. Importantly, learning rates were significantly modulated by the uncertainty manipulations: higher volatility produced elevated learning rates, and higher stochasticity led to reduced learning rates. Moreover, trial-by-trial analyses revealed that participants corrected for errors stemming from environmental stochasticity but did not adjust their behavior in response to errors attributable to internal motor noise. This dissociation indicates that participants effectively differentiated between external noise and motor variability when updating their actions.

In Exp 2, we investigated whether these adaptive responses are specific to tasks involving active motor control by introducing a non-motor variant of the air hockey game. Instead of physically moving the paddle, participants reported their intended release parameters—speed and direction—by clicking on a polar grid. Although the same wind manipulations were applied, an additional source of uncertainty was introduced by randomly varying the puck's weight, thereby approximating the noise structure of the motor task without engaging the motor system. Interestingly, in the non-motor task participants exhibited a faster learning rate compared to the motor task, but overall errors were larger. Moreover, participants in the non-motor context overcompensated for noise by conflating stochasticity with volatility, resulting in inflated corrective adjustments and increased response variability.

Together, these findings demonstrate that the human motor system is optimally tuned to parse and respond to multiple sources of uncertainty, including volatility and stochasticity and internal motor noise. In contrast, when motor engagement is removed, decision-making becomes suboptimal, leading to overcorrection and increased error.

G – Theoretical and Computational Motor Control

1-G-89 - Deep imitation learning for neuromechanical control: realistic walking in an embodied fly

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<u>Details</u>

Most walking animals can maintain motor control after limb injury or amputation, where coordinating movements of a drastically altered body requires dynamic interactions between the nervous system, the biomechanics of the body, and the physical environment.

Until recently, it has been challenging to link neural and biomechanical models to investigate adaptive motor recovery because it requires coupling neural control in closed-loop with the environment. Further, while previous approaches have been able to simulate walking in biomechanically realistic bodies, the joint kinematics and ground reaction forces have been unrealistic or unvalidated. In this project, we develop and train an agent with deep reinforcement learning (DRL) to imitate real \textit{Drosophila} walking using a biomechanically realistic fly body model in the physics simulator MuJoCo.

For training data, we use inverse kinematics to transform high-fidelity 3D keypoint data into 36 joint angle trajectories.

We show that our model closely resembles real fly walking while reproducing accurate movement dynamics (i.e. ground reaction forces).

Historically, measuring forces produced by such small animals has been impossible.

We validate our MuJoCo model with the first-of-their-kind measurements of ground reaction forces in freely walking fruit flies, demonstrating that simulated ground contact forces during walking closely match experimental measurements.

Using our validated walking model, we simulate locomotion after a front left leg amputation, and we show that force distribution per leg during walking significantly increases in the z-direction compared to normal locomotion.

More broadly, this work is a key step in using embodied agents to understand the neural mechanisms controlling robust movement with a dynamically changing body and environment.

1-G-90 - Error clamp behavior in visuomotor adaptation is not a singularity: challenges for modeling

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<u>Details</u>

We conducted a visuomotor rotation experiment in which subjects were instructed to either move their hand or the cursor to the target while experiencing a novel perturbation — a hand angle-gain — introduced alongside the standard rotation. This manipulation was inspired by the error clamp with one additional degree of freedom: by varying the hand angle-gain from one to zero, it is possible to introduce an error clamp condition in a graded manner. Our goal was to probe the effect of instructions under a partial error clamp condition.

A key finding of our study is that the saturation phenomenon associated with the error clamp is not an isolated behavior. That is, it is not a singularity among all visuomotor behaviours, arising only when the cursor angle is fully invariant to the hand angle. This has important implications for modeling. In particular, modeling standard learning and the error clamp as separate phenomena is questionable. The grand challenge is to develop a comprehensive model that can explain all observed visuomotor behaviours and not just individual phenomena. The poster will expose recently developed ideas from control theory that inform our modeling work.

1-G-91 - Control of internal dynamics in the transport of a complex object

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<u>Details</u>

Carrying a cup filled with coffee without spilling presents significantly more challenges than carrying an empty cup. The coffee inside the cup can exhibit unpredictable dynamics that the hand must correct or preempt to avoid spilling the coffee. Previous work on linear displacement of a 'cup of coffee', simplified to a ball rolling in an arc modeled as a cart with a suspended pendulum, highlighted that humans choose

initial conditions and control strategies to increase predictability and dynamic stability of the internal dynamics. The present study investigated curvilinear motion on a horizontal plane when moving the cup-ball-system. Horizontal motion necessitates to increase the model dimensionality from a simple to a spherical pendulum, shown as a ball rolling in a bowl, critically increasing the complexity of the ball dynamics.

Participants (n=15) controlled the virtual cup-ball system displayed on a large projection screen using a robotic manipulandum, with interaction forces transmitted through the robot handle. We tested two conditions: 1) ball rolls freely inside the cup, 2) ball fixed to bottom of cup (rigid body). In both conditions, participants moved the cup from a start to a target and back, passing through a via-point placed halfway. 5 different locations of the via-point enforced paths of varied curvature (20 ball-fixed trials, 50 ball-free trials for each via-point). Participants were instructed to move as fast as possible; in the ball-free trial without losing the ball. Dependent measures were path length, average velocity, forces acting on the system, and predictability, characterized by mutual information between interaction force and object movement. The forces were decomposed into their tangent and orthogonal components with respect to movement direction.

Expectedly, trials with the rolling ball proved more challenging as average velocity was lower compared to ball-fixed trials across all path curvatures. Interestingly, path length was longer in ball-free trials, indicating that participants either adjusted the path to the ball's movement, or that the ball dynamics deflected the cup from the intended motion. Expectedly, predictability, a measure of how consistently user-applied forces influence cup velocity, was lower in ball-free trials. Further, it decreased with increasing path curvature, suggesting that humans generate less predictable interactions with curvilinear motion where non-tangential ball forces increase. Participants also applied less force on the cup in ball-free trials: while this is partly due to lower average velocity, it is also a first indicator that user forces align with ball forces and thereby leverage them in movement direction. The latter results suggest that participants may not only contend with ball forces, but also exploit them during interaction.

<u>1-G-92</u> - Submovements and cognitive load: The effect of varying cognitive load on the production of submovements, and the effect of submovement rate on cognitive load

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Details

We observe multiple peaks in the velocity profile in any movement more complex than a quick point-topoint movement. One explanation for these peaks is that they result from submovements – a marker of intermittent control used to control movement. While there is controversy regarding whether movements are planned in the brain in terms of submovements, the rate of submovement production nevertheless remains a useful tool in quantifying motor performance, e.g., as a result of rehabilitation or motor learning. The cognitive cost of producing submovements has not been studied extensively. In this study, we examine the relationship between submovements and cognitive load in two directions. First, we show that increasing the cognitive load (using different levels of a dual-task) causes the submovement rate to increase when performing a straightforward tracking task. Second, we induced different submovement rates using a well-known manipulation - changing movement duration. We compared the differences in cognitive load caused by different submovement rates using the detection response task (DRT) as people performed a similar tracking task. Using the EZ-diffusion model, we found that the drift rate (i.e., how fast people accumulate evidence for a decision) was modulated by the submovement rate, with the drift rate being slower when more submovements were produced. Overall, these two studies further our understanding of the cognitive cost of generating submovements. Further, they suggest that the generation of submovements is not fully automatic, as it impacts cognitive load. It also demonstrates how submovement rate may be used to quantify cognitive load while performing continuous movements.

<u>1-G-93 - Loss of complexity in stroke-impaired spatiotemporal finger control revealed by reduced</u> <u>individual and task specificity</u>

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<u>Details</u>

Stroke survivors' hand function is often impaired, reducing the ability to perform daily activities. Able-bodied (AB) adults demonstrate complex kinematic finger coordination, as quantified using principal components analysis (PCA) (Yan et al., 2020). However, compared to AB adults, stroke reduces finger control complexity, requiring less principal components (PCs) to explain the same amount of variance in isometric fingertip forces during an individuated finger force production task (Xu et al., 2023). However, finger endpoint forces do not reveal how stroke impacts the spatiotemporal coordination of finger forces, which may better reflect stroke-induced neural constraints. Further, while kinematic finger coordination appears task-specific in AB adults (Yan et al., 2020), it is unclear how stroke affects the task- and individual-specificity of finger force coordination.

Here, we characterized the spatiotemporal complexity of post-stroke finger coordination and determined if the task and individual-specificity of force coordination is reduced post-stroke. We **hypothesized** that post-stroke neural and biomechanical constraints reduce finger force coordination complexity, leading to reduced task- and individual-specificity of these coordination patterns.

We recorded 3D isometric fingertip forces from 41 AB adults (30 young-adults (YA; 18-35 years), 11 older adults (OA; 55-85 years)) and 20 stroke survivors (paretic (P) and non-paretic (NP) fingers; 30-80 years). Participants produced individuated finger forces in six directions at four force levels (20, 40, 60, 80% of maximum voluntary force) (Xu et al., 2023). To identify individual-specific spatiotemporal coordination patterns, we applied PCA to each subject across all tasks. To determine if coordination complexity is reduced post-stroke, we compared the number of PCs required to explain 95% of force variance across groups. To determine if post-stroke coordination patterns were task and individual-specific, we used Linear Discriminant Analysis to classify tasks using PCs for each participant, separately (Yan et al., 2020), and classify participants using PCs from all participants performing the same tasks.

Paretic-hands **a)** required fewer PCs (7.8 \pm 1.6) than YA (10.0 \pm 3.0;p<0.01) OA (9.4 \pm 2.8;p=0.08) and NP-hands (9.4 \pm 1.8;p=0.012) to explain 95% of force variance, **b)** were less task-specific (classification accuracy=61%) compared to YA (93%; average across participants), OA (85%) and non-paretic hands (81%; all p<0.001), **c)** were less individual-specific (accuracy=51%; average across tasks) compared to YA (72%), OA (74%) and non-paretic hands (65%; all p<0.001). These findings suggest post-stroke neurobiomechanical constraints reduce spatiotemporal finger complexity, impairing the ability to generate forces needed for daily manual tasks. However, impaired coordination patterns may not be individual-specific, motivating future research into characteristic impairments to post-stroke finger coordination.

<u>1-G-94 - Neural properties underlying the efficiency-robustness trade-off in motor control: insights</u> <u>from RNNs</u>

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<u>Details</u>

Human reaching movements exhibit a fundamental trade-off between exploiting known dynamics versus defending against unexpected disturbances [1]. When reaching in predictable conditions, our movements resemble trajectories generated by an optimal feedback controller (OFC). However, when anticipating potential disturbances that we cannot precisely model, we adopt a more defensive strategy: reaching faster, responding more vigorously to sensory feedback, and becoming more resistant to perturbations. This strategy shift coincides with uncertainty in our model of the dynamics and is well-described by H-infinity robust control theory. While the behavioral signatures of this trade-off are well-characterized, the neural mechanisms implementing it remain unknown.

Here, we trained small (n=100 units) single-layer recurrent neural networks (RNNs) with a linear readout to perform straight, undelayed reaches of a point mass. To implement these experiments, we developed Feedbax (available at [2]), a library for training and analyzing neural networks in feedback control tasks. Using these tools, we showed that our RNNs naturally captured key features of the efficiency-robustness trade-off. Networks trained under higher levels of model uncertainty developed more robust control policies, showing the same behavioral signatures that distinguish robust from optimal control in theory and human experiments: greater peak forces and velocities, and higher feedback gains. Most notably, a single RNN learned a continuous spectrum of policies ranging from optimal to robust, controlled by a scalar input signaling the expected level of model uncertainty.

In networks implementing more robust policies, unit stimulation led to larger output forces, yet the network maintained smaller goal displacements through feedback compensation. The network's steady states formed a ring of fixed points in state space, reorganizing along a principal component as the uncertainty signal increased. Eigenvalues of the linearized dynamics collapsed toward the origin, indicating stronger convergence to these fixed points. These properties reveal how input reshapes network dynamics to achieve robust control through stronger stabilizing and feedback dynamics.

Our results suggest that variable robustness may not require a specialized neural architecture. Instead, a simple RNN can produce a full spectrum of control policies through systematic variations in its neural properties, guided by a scalar signal of model uncertainty. While we do not address how the brain might compute this signal, our work provides specific, testable predictions about neural activity patterns underlying the efficiency-robustness trade-off in motor control. More broadly, these findings suggest that local neural circuits throughout the brain might use low-level mechanisms to adjust their robustness with respect to each other's influence.

[1] https://doi.org/10.1523/JNEUROSCI.0770-19.2019

[2] <u>https://github.com/mlprt/feedbax</u>

1-G-95 - The temporal dynamics of physical fatigue and its meural mechanisms

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<u>Details</u>

Fatigue arises from physical exertion and diminishes with rest. Yet, the mechanisms by which exertion and rest interact to elicit this feeling and the neural processes underpinning them remain poorly understood. We developed a theoretical framework that quantifies the temporal dynamics of exertioninduced depletion and recovery in momentary feelings of fatigue. We conducted an fMRI experiment where 17 healthy young adults performed repeated hand grip exertion trials interspersed with rest periods while reporting their subjective fatigue levels. We modeled momentary subjective fatigue using a dual state-space model. In this model, fatigue dynamics were governed by two processes: a fast process that is sensitive to rapid fluctuations in fatigue from exertion and rest, and a slow process that gradually evolves and tracks more persistent feelings of fatigue. Each state was influenced by an adaptation rate controlling fatigue accumulation during exertion and a retention factor regulating its decay over time. We found that the right insula, a key region related to judgments of effort, is modulated by participants' momentary subjective fatigue ratings. The right insula is integral in detecting and processing bodily signals to guide decision-making and action. Importantly, we found that modulation in the anterior cingulate cortex (ACC) activity and middle frontal gyrus (MFG) activity was explained by the fast and slow processes of our model, respectively. The ACC is crucial for error detection, supporting its involvement in the fast, fluctuating component of fatigue. The MFG, is associated with executive control and sustained attention, and is likely involved in the slow, more persistent buildup of fatigue. These results provide neural support for the dual-process structure of our computational model, suggesting that distinct neural circuits are responsible for capturing the fast and slow processes of fatigue. Our subsequent fMRI analysis will investigate the functional connectivity between these regions to better understand the network of brain activity that underlies feelings of fatigue.

<u>1-G-96 - The average progression of learning can obscure multiple learning trends: A computational cautionary tale</u>

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<u>Details</u>

Neurorehabilitation is often modeled as experience-driven skill acquisition (i.e., a form of learning). While some researchers argue that sensorimotor learning is adaptable and influenced by prior experience (Zeidan,

2024; Shadmehr and Holcomb, 1997; Kitazawa et al., 1997), they often overlook the inherent variability in individual learning trajectories.

This study explores the emergence of multiple learning trends by moving away from averaging the progression of learning across individual trials. An iterative unsupervised clustering approach was guided by Silhouette score analysis that quantifies the degree of separation between clusters and ranges from - 1 to 1, where a high positive score indicates that the data point is well-matched to its own cluster and poorly matched to neighboring clusters Rousseeuw (1987). This enables identifying distinct learning trends within and across curricula, revealing differences in the progression of learning and final fitness . The learning process is structured around Proximal Policy Optimization (PPO), a reinforcement learning algorithm as presented in Ojaghi, Mir et al. (2024). We trained a simulated robotic hand to manipulate a ball

across five curricula when the task changes midpoint in learning: (1) lift followed by lift and rotation,(2) rotation followed by lift and rotation, (3) a baseline (i.e., no curriculum) where lift and rotation were

trained throughout the learning, (4) lift and rotation followed by rotation and, lastly (5) starting with lift and rotation before transitioning to only lift. This allows us to examine whether and how curricula shape learning progression. After performing 60 trials for each curriculum, we ran a two-level K-means approach to cluster the progressions of learning to have the average height of the final 10 seconds of each trial within 25% of the target height of 25 mm. By applying unsupervised clustering techniques, the research seeks to

identify and categorize distinct learning trends, moving beyond traditional performance averaging. Our findings indicate that multiple learning trends emerge from curriculum learning, challenging the notion of a single learning trend. The study identifies trends such as 'no learner,' 'steady learner,' 'saturate

high' and 'learn and drop,' each describing different progression paths. The results demonstrate that the average progression of learning can obscure multiple learning trends, and highlights the need for a nuanced evaluation of 'rehabilitative' trends (Valero-Cuevas et al., 2016).

<u>1-G-97 - A computational counterexample to the need for sophisticated tactile sensing when learning to manipulate</u>

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Details

Tactile feedback is considered to play a critical role in skill acquisition and adaptation, influencing grasping,

force modulation, and object manipulation (Wilson et al., 2016; Cienfuegos et al., 2024). This assumption has driven the engineering approach of emphasizing the inclusion of sophisticated tactile sensors in robotic and prosthetic hands (Abd et al., 2022; Dsouza et al., 2016). However, the ability of individuals to still manipulate objects effectively despite impaired sensation (such as when wearing gloves, in cold weather,

or with soapy hands) challenges the longstanding belief that tactile input is necessary (Johansson and Cole,

1994; Johansson and Westling, 1984; Nowak et al., 2001; Pavlova et al., 2015). This study challenges the assumption that high-fidelity tactile sensors are always necessary for effective learning in robotic manipulation.

Using a simulated three-finger robotic hand, the study examines whether advanced 3D-force sensing provides a distinct advantage over simpler tactile modalities such as Normal-force, Binary-contact, and No-tactile sensation. Additionally, by employing unsupervised clustering, we tested whether different levels of tactile feedback produce different learning trends.

The study extends previous research on in-hand manipulation simulating a robotic hand interacting with a ball under four different tactile conditions: No-tactile, Binary-contact, Normal-force, and 3D-force (Ojaghi*

et al., 2024; Mir et al., 2024). The learning process is conducted using Proximal Policy Optimization (PPO),

a widely used RL algorithm. Two experimental scenarios are explored: a Baseline condition where the task of lifting and rotation remains constant during the learning period, and a Curriculum learning condition where we start with lift and add rotation as a second subtask to the second half of the learning. After collecting 60 trials from each sensory input condition, we aggregate all the progressions of learning as a time series—from all tactile sensory input for each scenario—over each episode and run it

over a two-level K-means clustering approach to cluster progressions of learning. Surprisingly, higher-fidelity tactile sensors (i.e., 3D-force) do not necessarily improve learning outcomes ;

and learning can happen even in the absence of tactile sensory input (i.e., No-tactile). In fact, Binarycontact sensors performed comparably to 3D-force sensors, suggesting that basic contact information can be sufficient for effective learning. Furthermore, the clustering analysis revealed that distinct learning trends emerged across all types of tactile sensory input, demonstrating that tactile fidelity alone does not determine learning success. Future work is needed to clearly establish for which tasks and environments

this applies—and if so—which, when, and whether sensory information is needed during different phases of the learning process.

1-G-98 - Memory-sensory integration in skilled sequence production

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<u>Details</u>

In everyday activities, humans produce sequences of movements flexibly: While many are guided by memory, we often rely on sensory cues to adjust our actions. The processes by which the motor system seamlessly integrates these two sources of information remain poorly understood. Here, we address this question using a discrete sequence production (DSP) task, in which both memory and sensory cues jointly guide movement planning. Participants were trained on finger-keypress sequences and then tested on familiar (**Trained**), unfamiliar (**Random**) sequences. To manipulate the availability of sensory information, we changed the **Visible Horizon**, the number of cues that were displayed for future presses.

In random sequences, production time decreased as participants had bigger Visible Horizons, indicating concurrent planning of multiple future presses. Notably, this benefit persisted for trained sequences, where the memory of the sequence was present. This suggests memory and sensory information are **integrated** during planning, even though participants could have relied on memory exclusively. To ensure that participants can fully depend on their memory, a supplementary experiment will require participants to execute trained sequences depending solely on memory. We predict observing integrated use of memory and sensory information when available, though maybe to a lesser extent when having a stronger memory of the sequence.

To probe the interaction between memory and sensory information, participants were also tested on partially modified (**Trained-Changed**) sequences. In these trials, trained sequences were altered by randomly changing either a single digit or all digits following a certain position. Participants slowed down on the first press that deviated from the trained sequences. That press was even slower (and error rate was higher) than for random sequences. This suggests a conflict between memory expectation and sensory information that needs to be resolved. Surprisingly, although planning for the changed press began 2-3 presses in advance, earlier presses were unaffected, suggesting each item is planned and triggered independently. If the sequence returned to its trained order after the changed press,

participants remained slower for several presses. If all subsequent presses deviated from the trained sequence, the conflict disappeared immediately. This indicates that fully reactivating the sequence memory is not immediate, while it can be deactivated rapidly.

Our results suggest that individual sequence items are planned **concurrently** and **independently** and sensory and memory information are **integrated** in the planning of the items. When confronted with a conflict, memory **reactivation** is delayed while memory **deactivation** occurs immediately. We show that these observations can be accounted for by a computational model that consists of multiple, parallel occurring drift-diffusion processes—each dedicated to planning an individual sequence item.

<u>1-G-99 - Unsupervised generative model for neural-drive estimation through real-time spike detection</u> <u>in low-density surface EMG interfaces</u>

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Details

Current modalities in the field of motor control exploit raw EMG signals recorded through surface electrodes. These signals are normally processed through various feature-extraction methods, either computing common time and frequency-based features, or exploiting neural networks to extract more specialized patterns from EMG data.

While effective, these approaches provide only a coarse estimation of the neural drive to muscles and are primarily used in relatively simple gesture-recognition tasks.

To improve neural drive estimation, decomposition algorithms have been developed to identify discharge times of superficial motor units, extracting single motor-neuron spike trains from high-density surface EMG.

These algorithms, however, are computationally expensive, require high-density electrode configurations, can only be used during isometric contractions, and real-time applications rely on tracking pre-identified motor units, which are easily lost over short periods of time.

Moreover, individual motor units only partially encode the full neural information transmitted by the brain, and their separation represents an unnecessary step for estimating the neural-drive, which is more accurately approximated by the compound activity of the different motor neurons, namely the cumulative-spike train (CST).

This study presents a novel generative architecture capable of accurately estimating the discharge times of groups of motor neurons from each EMG channel.

This has been validated on both real and simulated data, demonstrating significantly better performance than standard spike-detection algorithms and achieving CST estimates comparable to decomposition algorithms. It has also been shown that the model learns to approximate each input channel as the convolution of the estimated spike train and an average motor-unit-action-potential (MUAP) shape.

Lastly, the model is adaptable to different electrode configurations (including single-channel setups), is trained in an unsupervised manner, and does not require isometric contractions.

This allows to overcome the limits of standard decomposition algorithms, enabling fine motor control and accurate neural-drive estimation in online scenarios, with potential applications in human-motor augmentation studies (e.g. real-time analysis of cortical beta projections to muscles).

1-G-100 - Interaction between motor adaptation and arm choice in virtual reality

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Details

The decision to use one arm over the other is a frequent, almost automatic part of daily life. Arm choice has been modeled as a competition between values based on the relative costs (e.g., effort, movement time) associated with each arm. The non-use phenomenon in stroke reveals a gap in our understanding of arm choice. Rehabilitation may improve arm function without necessarily increasing arm use, raising questions about why individuals make choices that do not seem to maximize value. Following a stroke, arm movements become slower, more variable, and require more effort, with one arm affected more than the other. As individuals re-learn to move with the arm, their decision-making is influenced because the value of using the arm changes as the perceived costs and rewards are updated based on performance. Over time, new habits are established but the mechanisms behind this adaptation are unclear.

Decisions result from the deliberation of the goal-directed and the habitual systems. The goal-directed system relies on evaluating the costs and rewards of each action by mentally simulating the competing movements with internal models of the arms. The habitual system relies on learned behavior patterns that bypass detailed evaluation. In daily life, we make choices between our arms more out of habit, drawing from caches of arm values, rather than deliberate planning.

Motor adaptation to perturbations, whether from stroke or environmental changes, involves updating an internal forward model to reduce errors. The nature of the perturbation—whether introduced suddenly or gradually—can affect motor learning and decision-making. It has been proposed that movement errors are externally attributed to the experimental setup during an abrupt perturbation but internally attributed to the arm during a gradual perturbation. Following an abrupt change in the environment, large prediction errors cause the goal-directed system to take a more prominent role in decision-making to adapt rapidly to the new environment. Decisions become quicker and more habitual with extensive training.

We perturbed the dominant arm of healthy participants, recruited online, by introducing a cursor rotation in a Virtual Reality environment relative to the hand's movement. Abrupt rotations simulated sudden motor deficits, while gradual rotations simulated progressive impairments. During an abrupt perturbation, the externally attributed error requires remapping the target and changing the movement goal, so the expected motor cost for the newly updated target location is changed. In contrast, during a gradual perturbation, the internal model of the arm will be updated requiring no change in the movement goal from which the costs are computed. Preliminary results show that change in arm choice is minimal during a gradual perturbation and larger during an abrupt perturbation. Changes in reaction times reflect a shift in decision-making strategies.

<u>1-G-101 - Toward intention-driven neuroprostheses: Using eye fixations to predict joint moments in upper limb movements</u>

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Details

Being able to control upper limb neuroprostheses based on the user's intention can be highly valuable for enhancing the technologies' effectiveness and the user's independence. In this light, eye fixations on a location of functional interest – e.g., the location of a cup to be picked up – may provide valuable information for upper limb movement planning and, ultimately, for predicting upper limb moments needed for the control of neuroprostheses. Motivated by these considerations, **the overall goal of this study** was to predetermine joint moments for *future* actions within a functional upper limb task based on *current* eye gaze information from eye tracking. **Our specific objectives** were to: (1) use eye fixations to reliably identify future hand locations of functional interest; (2) use present and future hand locations of functional interest; e.g., when reaching for a cup) and validate them against actual hand trajectories; and (3) predict the upper limb moments from the modeled hand trajectories and validate them against the biomechanically determined joint moments.

15 non-disabled individuals were asked to perform the *Pasta Box Task*, a well-established functional upper limb task for studying and assessing upper limb performance. A gold-standard motion capture system was used to track the motion of the upper body, whereas a high-end binocular eye tracker was used to capture the eye kinematics during task performance. Post-experiments, all data were processed within our *Gaze and Movement Assessment (GaMA)* software, which allows us to clean the data and segment them into Reach-Grasp and Transport-Release phases of the various task movements. By synthesizing information from head kinematics, eye tracking, and pre-experiment calibrations, we also constructed a *three-dimensional (3D) gaze vector* that captures the participant's eye gaze in the 3D task environment. Post-processing, 3D eye fixations were identified and used to determine future object grasp or release locations, allowing us to quantify current and future hand locations for each Reach and Transport segment. We used 3-point Bezier curves to model the trajectories from current to future hand locations and validated associated upper limb joint angles (obtained via inverse kinematics) and moments (obtained via inverse dynamics) against those derived through standard biomechanical techniques.

Our results demonstrate that we are able to model biomechanically feasible hand trajectories for future upper limb actions using 3D gaze vector information and that the underlying joint moment profiles and magnitudes are comparable to those obtained directly via motion capture data. To assess the value of these results in a practical context (e.g., for use in neuroprostheses), future work will explore whether comparable results can be obtained with a minimal set of sensors, e.g., an eye tracker and two inertial measurement units on the head and hand.

<u>1-G-102 - Working memory capacity limits human temporal credit assignment during motor</u> reinforcement learning

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<u>Details</u>

In motor reinforcement learning (RL), temporal credit assignment (TCA) involves determining the optimal policy for selecting a sequence of actions based on reward feedback received only after the sequence is completed. Theoretically, TCA requires the learner to retain the action sequences in

memory so that they can update their policy, as in Monte Carlo learning or temporal difference learning with eligibility traces. Previous studies show that precision in human working memory decreases with the number of items that must be remembered (e.g., spatial locations). We hypothesized that working memory capacity may be a key bottleneck for TCA in motor RL. To test this idea, we designed a multistep reaching task in which human subjects moved their hand across a set of horizontal bars and attempted to maximize a reward score determined by the loss in each step, defined as the distance between the location where the cursor crossed the bar and an invisible target location. Between two conditions (N = 18 each), we varied the number of bars (2 and 4). We found that both the deviation from the target and the variance of the crossing locations on each bar were significantly higher in the 4-bar condition by the end of learning (100 trials). To explain this difference, particularly the higher uncertainty (variance) in the 4-bar condition, we developed a Bayesian Actor-Critic model. Similar to traditional Actor-Critic models, the learner maintains an expected reward value and adjusts their estimated target locations in each trial, either toward or away from the actual crossing locations, based on whether the received reward is higher or lower than expected. However, the amplitude of the adjustment follows a Bayesian update rule such that it is proportional to the relative amplitude of the uncertainty in the estimated target locations, maintained across trials, and the uncertainty in remembered crossing locations within a trial (observation uncertainty). The uncertainty for estimated target locations is also updated in a Bayesian manner, with a process uncertainty term (capturing the short-term memory decay for the estimated target locations) added in each trial. Together, the observation and process uncertainties contribute to the total uncertainty in target location estimates. Group-level model comparison results showed that the higher observation uncertainty in the 4-bar condition relative to the 2-bar condition significantly accounted for the behavioral differences, while no significant effect of the process uncertainty was found. Therefore, we infer that working memory capacity related to precision with which action sequences can be remembered is an important limiting factor for TCA in multi-step motor RL.

Poster Session 2

A – Control of Eye & Head Movement

<u>2-A-1 - Age-related differences in gaze distribution during locomotion: prioritizing safety or exploration?</u>

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Details

During locomotion, attention must be dynamically allocated to balance the need for gathering relevant environmental information while ensuring a stable gait. Gaze allocation is key to maintaining this balance between exploration and safety. For older adults in particular, fall prevention plays a critical role in locomotion. Prioritizing gaze toward the ground has been proposed as a compensatory strategy to enhance gait stability in older adults.

In this study, we investigated age-related differences in gaze allocation during locomotion, with and without an additional motor task. Specifically, we examined gaze behavior in both a real-world setting and a virtual reality (VR) environment to assess the comparability of behavior across these conditions. We recruited two age groups: younger adults (N=24, M=26.1 years) and older adults (N=24, M=68.8 years). Participants walked down a real hallway as well as a highly realistic virtual replica of the same

hallway. In both environments, they performed locomotion either as a standalone task or while engaged in an additional visual search task that required them to locate and manipulate small target objects positioned on the walls. To capture gaze behavior, mobile eye-tracking glasses were used in the realworld condition, while an integrated eye-tracking system within a VR headset was employed for the virtual environment. Our findings revealed a pronounced age-related bias in gaze allocation, with older adults displaying a strong preference for directing their gaze toward the floor. This bias was evident in both real-world and virtual locomotion conditions, supporting the notion that older adults prioritize gaitrelated visual information, likely as a compensatory mechanism to stabilize postural control. However, when a secondary motor task was introduced, older adults exhibited a notable shift in gaze behavior, reallocating their visual attention away from the floor and toward task-relevant information. This shift resulted in gaze allocation patterns that closely resembled those observed in younger adults, suggesting that, under certain conditions, older adults may flexibly adjust their gaze behavior—potentially at the expense of gait stability.

These findings have important implications for understanding the mechanisms underlying age-related changes in locomotion and attention. They suggest that older adults' prioritization of safety is not entirely rigid but can be influenced by competing attentional demands. However, this adaptability may come at a cost, as shifting attention away from gait-related information could increase the risk of instability and falls. We conclude that task demands during locomotion may critically compromise gait stability in older adults. Furthermore, gaze allocation appears to be similarly modulated in both real and virtual environments, supporting the validity of virtual approaches as a reliable proxy for investigating real-world locomotion control across the lifespan.

<u>2-A-2 - Prosthesis stimulation and the flocculus activity for Compensatory Saccade during the head</u> <u>impulse test in the vestibular impaired monkey</u>

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<u>Details</u>

The vestibulo-ocular reflex (VOR) plays a critical role in gaze stabilization. Patients with vestibular loss cannot maintain their gaze on a target during head movement because the gaze moves with the head movement away from the target. The head-impulse test (HIT) detects this unstable gaze. In this test, a patient is asked to fixate on a target and the head is rapidly and unexpectedly rotated to stimulate targeted semi-circular canals. Patients with vestibular loss make two types of compensatory saccades during HIT, covert saccades and overt saccades. Covert saccades occur during head rotation, whereas overt saccades occur after the head has stopped moving. A patient who has acquired covert saccades shows an improvement in the Dizziness Handicap Inventory score, higher visual acuity, and less oscillopsia. This may be because the displacement of the visual image is decreased by the saccade. Also, vision is greatly diminished during the saccade so the retinal slip is perceived less. Thus, learning to generate covert saccades is important for improving the patient's quality of life. To study the neural basis of these movements, we investigated saccade behavior during HIT in vestibular impaired monkeys and demonstrated that the monkeys made covert saccades.

To investigate the neural mechanisms in inducing covert saccades, we recorded unit activity from the right flocculus (a cerebellar cortical region that encodes vestibular signals) during HIT. We also stimulated the right horizontal semicircular canal with a vestibular prosthesis to attempt to facilitate covert saccade occurrence.

We found that flocculus neurons exhibited a burst of simple spike activity for ~200ms after HIT onset and a pause later during ipsiversive covert saccades. For ipsiversive overt saccades, the simple spike did not exhibit a burst. For contraversive covert and overt saccades, there was little phasic simple spike activity. Complex spikes discharged for both ipsi- and contraversive retinal slips. We also found that vestibular neuroprosthesis stimulation facilitated contraversive covert saccades but not ipsiversive covert saccades.

The results of the recording experiments suggest that the mechanisms to induce covert saccades are fundamentally different from those of overt saccades. We speculate that the burst of simple spikes suppresses the vestibular nucleus neuron's activity and, in turn, facilitates agonist activity and suppresses antagonist activity. Thus, flocculus neurons may be involved in assisting covert saccades. In addition, the pause of simple spikes suggests that the covert saccade command signal is created outside of the flocculus. The firing of the complex spikes during covert saccades was unexpected, since it fires for contraversive retinal slip predominantly in the normal monkey. The results of the neuroprosthesis experiments suggest that vestibular prosthetic stimulation may be able to enhance recovery through facilitation of covert saccades.

2-A-3 - Differential effect of reward and sensory errors on saccade adaptation and associated mislocalization

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Details

Accurate saccadic eye movements are a prerequisite for efficient exploration of and interaction with our surroundings. Our fovea, the area of sharpest vision, must be aligned with objects of interest to gather visual information that informs upcoming motor actions. Consequently, our eye movements are not only essential for the visual perception of our environment but also for the successful execution of goaldirected movements in a dynamic environment. This view on eye movements highlights their relevance for behavioral goals. Consequently, saccade accuracy can be understood in two ways: 1) A saccade is accurate if it produces its expected sensory consequences and the corresponding post-saccadic sensory error is zero. 2) A saccade is accurate if it is suitable to obtain a reward or achieve a behavioral goal and the corresponding post-saccadic reward error is zero. Usually, the post-saccadic sensory error and reward error match, making it difficult to study their differential contribution to the oculomotor learning process. However, in a recent eye-tracking study, we induced conflict between reward and sensory errors. The error signals were derived from the post-saccadic image: an intra-saccadic shift of an object array, consisting of three objects of different shapes, was combined with a color swap of the objects within the array. A verbal instruction determined the relevant target feature and, hence, the target object. The saccade amplitude was adjusted such that it landed on the task-defined target object both in case of congruent and incongruent post-saccadic information, indicating that saccade motor performance was adjusted to nullify the reward error. At the same time continued exposure to a sensory error led to object mislocalization, indicating that the oculomotor map adapted regardless of the executed saccade or incongruent reward errors. We conclude that saccadic adaptation involves both reward and sensory errors. While the former directly adapts saccade metrics to the current task, the latter updates the representation of objects in space.

2-A-4 - Eye movement abnormalities during visually guided reaching in subacute stroke participants

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Details

Background: More than 50% of stroke survivors experience visual problems following a stroke. Visual information is crucial to perform reaching movements. Reaching generally requires looking at the object one is reaching to and adjusting the motor command to the environment and the object. However, little is known about oculomotor behaviours during visually guided reaching in stroke participants.

This study **aim** was to describe eye movement behaviours in stroke survivors compared to a control group of participants during a visually guided reaching task.

Methods: Participants performed a visually guided reaching task using a robotic device with an integrated eye tracking system (Kinarm exoskeleton, Ontario, Canada). Participants made 20 cm reaching movements from a central target to one of two peripheral targets (1cm radius; target order pseudorandomized) on a horizontal display. The location of the index fingertip of the reaching arm performing was displayed as a white circle (0.5cm radius). We characterized saccadic eye movements during reaching with three spatial and three temporal eye movements parameters: (1) the accuracy of the first saccades made during the reach, (2) the accuracy of all saccades, (3) the variability of eye movement accuracy, (4) the first saccade latency, (5) the first saccade duration, and (6) the peak velocity of the first saccade. Data for the eye movements of the control group were used to build a linear regression model and adjust for sex, age, and handedness. Stroke participants were identified as abnormal if they fell outside of the 95% confidence intervals values.

Results: Fifty participants in the stroke group (age: 55.6 ± 14.3 years; 26 with right-side impairment; time post-stroke: 45 days) and 105 participants in the control group (age: 47.1 ± 17.4 years; 96 right-handed) performed the visually guided reaching task with their affected side (stroke) or non-dominant arm (control). All stroke participants were less accurate in their first saccades made during the reach, 38% were less accurate throughout the entire reach, and 30% exhibited greater variability than the control group. For the temporal parameters, 40% of stroke participants had a longer first saccade latency, 92% had a longer first saccade duration, and 36% showed abnormal peak velocity (with either excessively fast or slow peak saccadic velocity) compared to the control group.

Conclusion: Our results showed that all stroke participants exhibited abnormal eye movements in at least one spatial parameter, and more than 90% had abnormalities in temporal parameters. These findings highlight the importance of assessing oculomotor behavior during motor tasks, as such abnormalities could contribute to motor impairments and affect recovery. Analyses of the reaching movements are pending.

<u>2-A-5 - The role of visual interaction in movement coordination among wind instrument ensemble</u> <u>musicians</u>

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<u>Details</u>

Ensemble musicians visually interact with each other through eye contact, gestures, and body movements during musical performances. Visual interactions facilitate the synchronization of timing and tempo in ensemble performances, enhancing expressive coordination and providing significant benefits
for both performers and audiences. A previous study investigated how restricting visual information affects the head movement in ensemble musicians. The results showed that when visual information was limited, the amount of head movement decreased, suggesting that necessary visual interaction in ensemble performances was reduced. However, their study focused only on changes in the head movement and did not examine the motor coordination among performers when visual information was limited. Therefore, the present study aims to evaluate the relationship between visual information manipulation and motor coordination in skilled wind ensemble musicians.

We recorded performances of three professional or semi-professional wind ensembles using a markerbased optical motion capture system. Each ensemble performed under two conditions: (1) visual interaction, in which musicians faced each other for visual communication and performed naturally with typical musical expressiveness and eye contact; (2) non-visual interaction, in which musicians were positioned so that they could not see each other, minimizing visual interaction while performing as naturally as possible. Following several previous studies measuring movement coordination in ensemble performance, this study examines performers' head velocity as coordination indicator. The head movement velocity was calculated from three-dimensional marker displacement on the top of the head. To evaluate the movement coordination, we applied cross-wavelet transform (CWT) analysis. The time windows were aligned with musical phrase structures ranging from one beat to four bars. The CWT power represents the coordination strength. Furthermore, to evaluate the similarity of head movement patterns over time, we applied Dynamic Time Warping (DTW), where the DTW distance represents the time-series similarity. Since both CWT and DTW are pairwise analyses, we conducted them for all possible performer pairs within each ensemble. Ensemble-wide CWT power and DTW distance were then obtained by averaging values across all pairs.

Results showed no significant differences between the visual interaction and non-visual interaction conditions in both the phrase-related coordination (CWT power) and the head movement similarity (DTW distance). These findings suggest that visual interaction may not play a crucial role in the motor coordination of wind instrument players. Future studies may gain deeper insights by measuring performers' eye movements and examining how visual interaction influences performance quality.

2-A-6 - Hand-eye coordination: a dual model predictive control theory

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<u>Details</u>

Understanding the coordinated motion planning and regulation of eye and limb movements is essential for predicting human actions. While numerous models of either eye or arm movements have been developed, they cannot predict how changes in limb dynamics affect eye movement or, conversely, how variations in visual information quality impact limb control. In particular, eye gaze models have predominantly focused on intent classification using machine learning techniques, lacking clear principles to predict how humans coordinate eye and hand movements or how changes in limb dynamics and visual information quality influence this coordination.

We address this gap by modelling the eye and limb as two interacting systems, each governed by distinct control strategies, defined by individual cost functions. Specifically, we propose a stochastic model predictive control (MPC) framework that captures the central nervous system's capacity to predict, plan, and correct movements based on the dynamics and noise models of both the sensorimotor system and the external environment. The two systems are connected by the estimation

of the target trajectory and its associated uncertainty: the eyes move to gather information to update the target estimation, while the hand plans its motion based on it.

We evaluated the proposed framework with a trajectory-tracking task, performed by controlling a cursor using wrist flexion/extension movements. The trajectory to follow is displayed over a 2 s sliding time horizon, thereby providing participants with information to plan their hand motion. This task enforces a continuous target trajectory that allows us to investigate the frequent (re)planning and coordination mechanisms as a function of task difficulty and the time horizon of visual information. The results showed that the participants looked at a constant horizon of about 200 ms in future, with a pursuit-saccade pattern, whose frequency depended on the sliding velocity. Simulations using our dual MPC approach predict the experimental data well, with a smooth hand movement and a saccadic eye movement that maintains a constant average horizon.

The new framework integrates eye and limb motor control, providing a structured, generalizable approach to studying their coordination. It opens the way to principled methods for predicting human motion intention from eye gaze that can be readily integrated into existing human-robot interaction paradigms.

B – Fundamentals of Motor Control

2-B-8 - Cortical correlates of tactile suppression during active and passive movements

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Details

Tactile sensitivity on a limb is diminished during voluntary movements. This phenomenon is known as tactile suppression, and has been attributed to central and peripheral mechanisms. Central mechanisms can drive suppression via internal forward models in which predictions of upcoming movement consequences are used to down-regulate actual sensory feedback caused by the movement. Peripheral mechanisms can drive suppression via masking of weaker tactile sensations by stronger sensations arising from the movement. However, it is still unclear how central, motor predictions and peripheral feedback processes are implemented in the human brain. Here we investigated the neural underpinnings of tactile suppression of external stimuli by addressing the relative contributions of predictive and peripheral processes.

We used fMRI to measure cortical activation within the sensorimotor network as participants (N=29) received brief vibrations of varying intensities on their right ring finger, probing tactile sensitivity, shortly before moving their right wrist either in an active or passive manner. During active movements participants moved the handle of a pneumatic device whereas during passive movements, the handle of the device was moved by air-pressure, without participant's intention. We reasoned that during active movements, both central and peripheral mechanisms play a role in movement-related tactile suppression whereas for passive movements, it is peripheral feedback that primarily impacts tactile sensitivity during movement. Resting trials, in which identical tactile stimuli were presented on the finger without movement, served as a baseline. In half of the trials, no tactile stimulus was presented. Participants reported after each movement whether they detected a vibration (yes/no task). We calculated tactile sensitivity using signal detection measures that take into account false alarms. Whole-brain univariate analyses were conducted using a two-stage general linear model. Each participant's

data was initially fitted to a fixed-effects model, and regressors defining movement-by-stimulation interactions were passed to a random-effects model at the group level.

Active and passive movements resulted in decreased tactile sensitivity compared to baseline. Univariate fMRI results (final N = 27) indicate that BOLD activation associated with tactile stimuli was modulated by movement, in different somatosensory regions. Specifically, relative to tactile stimuli presented in the absence of movement, tactile stimuli during active movements led to BOLD deactivations in the left primary somatosensory cortex (SI), contralateral to the moving effector. In contrast, tactile stimuli during passive movements resulted in BOLD deactivations in the left secondary somatosensory cortex (SII) compared to resting.

Active movements led to BOLD deactivations in the SI, likely reflecting motor predictions that suppress sensory input, while passive movements led to deactivations in the SII, potentially reflecting peripheral masking of weaker sensory signals. Functional connectivity analyses will further investigate the relative contributions of motor prediction and peripheral feedback in these regions by examining the connectivity between somatosensory (SI, SII) and sensorimotor regions implicated in sensorimotor prediction and integration (supplementary motor area, anterior cerebellum, posterior parietal cortex). Our results indicate distinct contributions of central, predictive and peripheral mechanisms to tactile sensitivity during movement, at different levels of the somatosensory processing hierarchy.

<u>2-B-9 - The sitting position at work: comfortable but not optimal for perception, attention, decision</u> <u>and performance</u>

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Details

For several million years, our early and recent ancestors were nomadic. Our predecessors only became sedentary relatively recently in history. Since World War II, various factors have led individuals to sit increasingly more: improved conveniences (e.g., TV, washing machines, dryers, dishwashers, bread makers), technological advancements and innovations (modern transportation, ergonomic chairs, hightech devices). More recently, the Internet and communication media have further changed our habits, increasing the time spent sitting. Additionally, the pandemic COVID-19 and its consequences (e.g., increased reliance on teleworking) have further amplified the time spent seated. Today, more than half of the world population, particularly in high-income countries, spends over 8 hours per day sitting more than half of the waking day. This raises the question: is excessive sitting beneficial or detrimental to task performance (for short-term tasks), work productivity (for long-term tasks), and, more broadly, health? Publications from the 20th century largely suggest higher performance, productivity, and health when sitting compared to standing. However, the time spent seated has now reached unprecedented levels. A first review of the literature shows that work productivity is negatively impacted by excessive sitting. Studies even indicate that alternating between sitting and standing using sit-stand desks positively affects various aspects, including enthusiasm, comfort, alertness, attention, and performance. A second review highlights that task performance in various (short) desk-based tasks is generally equal (in most cases), sometimes better (notably for tasks requiring reaction time), and never worse when standing compared to sitting. Three recent studies from our group (under review or in progress) confirm faster reaction times when standing than when sitting for both short-term and medium-term tasks. Importantly, in our view, this benefit does not stem from standing itself but rather from the act of swaying while standing. This movement positively influences perception, attention, and task

performance (Bonnet and Viseux, submitted for publication). This hypothesis challenges most existing models of posture and motor control. According to our perspective, swaying and actively maintaining balance enhance attention, perception, and task performance, as long as standing does not lead to fatigue or pain. In our view, both insufficient and excessive postural sway are detrimental to performance in goal-directed tasks, while a moderate degree of sway (close to the one in quiet stance) is optimal. A review of the literature supports this sway trade-off hypothesis, as ten publications have already demonstrated that postural sway enhances task performance in affordance-based tasks. A recent study from our group aligns with these findings. Our article sets out the case for standing and swaying in our world.

<u>2-B-10 - Effects of transcutaneous vagus nerve stimulation on motor reflexes elicited by mechanical perturbations during reaching movements</u>

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Details

Mechanical perturbations during reaching movements elicit short latency (SL) and long latency (LL) reflexes, occurring approximately 20-50 ms and 50-100 ms after the perturbation, respectively. While SL reflexes are mediated at the spinal level, LL reflexes are modulated by cortical and cerebellar structures, making them particularly sensitive to task requirement. For instance, LL reflex amplitude is greater when reaching toward narrow targets, which require strict control, compared to wide targets, where precision demands are lower, reducing the need for corrective responses to perturbations.

The locus coeruleus-norepinephrine (LC-NE) system projects to much of the brain, including motor cortex and cerebellum, yet its role in shaping control processes underlying reaching movements remains poorly investigated. Here, we applied transcutaneous Vagus Nerve Stimulation (tVNS) in humans to causally probe the role of LC-NE system in refining control policy during perturbed reaching movements. We hypothesized that, compared to sham stimulation, tVNS would amplify LL reflexes for narrow targets, where precision is task-relevant, but not for wide ones, where it is task-irrelevant, aligning with LC-NE theories suggesting its role in allocating resources to task-relevant processes.

Twenty-five young healthy right-handed participants (23.8 ± 2.6 years old; 16 women) performed rightarm forward reaching movements toward narrow or wide targets, alternating across blocks. Each trial began with a 4-second train of either sham or active tVNS, alternating every other block. In 67% of trials, a mechanical perturbation was randomly applied to the left or right, eliciting reflexes in the right Posterior Deltoid (PDelt) or Pectoralis Major (PectM), respectively. Pupil size as marker of the effect of tVNS, and movement kinematics were also measured.

As expected, SL and LL reflexes were elicited in the PDelt and PectM when these muscles acted as agonist in response to perturbations, with the LL component being larger for reaches toward narrow targets compared to wide ones in both muscles. Trains of tVNS significantly increased pupil size, consistent with LC-NE activation. As hypothesized, this activation enhanced task-relevant LL reflex during narrow-target reaches compared to sham stimulation. Notably, this effect was observed only in PDelt (leftward perturbations), and not PectM. Additionally, PDelt exhibited greater baseline activity during tVNS compared to sham blocks, an effect that was specific for narrow target and developed over the course of a block.

Altogether, these findings suggest that tVNS-induced LC-NE activation modulated LL reflexes in a manner consistent with task-dependent adjustments of the control policy. Surprisingly, this modulation extended to muscle activity before movement execution, calling for further investigation into the LC-NE system's role in motor preparation.

2-B-11 - Improved error labeling in generative motor sequence learning

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Real-world motor skills are often composed of precise spatiotemporal action sequences that are characterized by a speed-accuracy tradeoff. That is, skill expertise is expressed when the action sequence is performed at high speeds with extremely few errors. Skill learning is often studied in the laboratory using tasks where participants are instructed to type sequences of keypresses as quickly and as accurately as possible. One version is the serial reaction time task (SRTT), in which individual actions are cued before participants respond. When either a deterministic or probabilistic sequence is embedded in the cue ordering, participants are able to implicitly learn the sequence structure through repetitive practice and improve their performance relative to random ordering of cues. Errors in the SRTT are simply defined as mismatches between the cued action and the response, and are all classified as "substitution" errors.

For many real-world skills however, performers have *a priori* knowledge of the sequence structure and are required to generate the full sequence. For example, pianists play from sheet music or recite well-known music from memory. Individual errors present in generated action sequences can be one of three types: 1) substitutions (i.e. – playing the wrong note), 2) insertions (i.e. – playing an extra note) or 3) deletions (i.e. – omitting a note one was supposed to play). Importantly, these different types of errors may be related to different underlying neural processes.

The sequential finger tapping task (SFTT) is a widely used laboratory task that investigates this type of skill learning. A symbolic target sequence is displayed on a visual display (similar to sheet music placed on a stand), and participants are instructed to type the sequence as fast and as accurately as possible over a predetermined practice trial duration or number of sequence iterations. The predominant approach for labeling errors in the literature has been utilized pattern matching of the fixed target sequence on the display to the generated sequence (FIXED pattern matching) [1], with only a single attempt made to label error types limited to cases where error density was extremely low (<0.0325) [2].

In the present study, we simulate generated sequence data containing errors of different types with varied density and spacing between multiple erroneous keypresses. First, our results show that error labeling with FIXED pattern matching suffers from a high false-positive rate. Next, an alternative pattern matching approach recently introduced in Buch et al. (2021) [3], which utilizes all possible circular shifts of the target sequence (CIRCULAR pattern matching), reduces the false-positive rate substantially for isolated errors, but displays a drop in accuracy as error density increases and the inter-error distance is between one-half and three-quarters of the target sequence length. Finally, we introduce a new approach (GENETICS) that utilizes the Needleman-Wunsch algorithm originally developed for genetic sequencing applications [4]. We show that the GENETICS approach more accurately labels errors (including error type) across a broad range of error densities and spacing.

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<u>2-B-12</u> - Disentangling the effects of inhibitory control and reward prospect on decision urgency and <u>corticospinal excitability</u>

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<u>Details</u>

INTRODUCTION: A recent transcranial magnetic stimulation (TMS) study¹ revealed that fluctuations in urgency during decision making are accompanied by modulatory shifts in corticospinal excitability of distant task-irrelevant muscles (CSE-DTIM), with CSE-DTIM decreasing in parallel with reduced urgency. However, due to the study's design, it remains unclear whether this decrease in CSE-DTIM was driven by increased inhibitory control, as originally suggested, or instead resulted from lower reward prospects, as both elements characterized conditions where urgency was reduced. Here, we independently manipulated inhibitory control requirements and reward prospects, allowing us to disentangle their respective contributions to CSE-DTIM suppression during decision making.

METHODS: Twenty young healthy right-handed participants (24.2 ± 3.2 years old; 13 women) performed an index finger variant of the Tokens task while TMS was applied over the primary motor cortex to elicit motor evoked potentials in task-irrelevant left leg muscles, serving as a measure of CSE-DTIM. Trials were randomized within blocks requiring either low or high inhibitory control, based on the distribution of trial types, and were associated with either a low (1 cent) or high (10 cents) reward upon success, resulting in four experimental conditions. Several behavioral measures were recorded, including decision duration and accuracy. Moreover, to quantify overall urgency in each condition, we computed the urgency intercept using the urgency gating model². Additionally, impulsivity was assessed using the UPPS questionnaire, and individual scores were included as covariates in the single-trial analyses of behavior, urgency and CSE-DTIM, conducted using linear and generalized mixed models.

RESULTS: Overall, decision duration and accuracy data suggest that inhibitory control was recruited according to its demands in each block type, with higher reward prospects generally enhancing this recruitment. Moreover, both reward prospect and inhibitory control requirements influenced the urgency intercept, with effects varying according to impulsivity scores. In less impulsive participants

(lower scores), urgency primarily varied with changes in inhibitory control demands, decreasing with higher inhibitory requirements, and this was accompanied by a suppression of CSE-DTIM, especially in high reward trials. In contrast, in more impulsive participants (higher scores), urgency was primarily modulated by reward prospect, decreasing when reward was higher, regardless of inhibitory control demands, presumably to optimize reward acquisition. Crucially, here too, CSE-DTIM also followed the decrease in urgency, being lower in high-reward trials.

CONCLUSION: These findings suggest that less impulsive individuals recruited inhibitory control according to the task demands whereas more impulsive individuals did so when it increased their chances of obtaining a high reward. In both cases, inhibitory control recruitment was linked to greater CSE-DTIM suppression, even when associated with a high reward prospect. This suggests that CSE-DTIM suppression is more likely driven by inhibitory control than low reward prospects, as initially questioned based on our previous study.

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²Cisek, P., & Thura, D. (2022). Models of decision-making over time. The Oxford Research Encyclopedia of Neuroscience. <u>https://doi.org/10.1093/acrefore/9780190264086.013.346</u>

2-B-13 - Multichannel electrode neuronal spinal cord recordings on behaving nonhuman primates

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Details

Spinal circuits perform complex adaptative sensorimotor transformations. However, the number of studies addressing the properties of the spinal cord circuits is relatively modest compared to other regions such as cortex or basal ganglia where new technologies such as multichannel electrodes (ME) have allowed to obtain wider and more detailed knowledge of neuronal functions by the simultaneous recording of many neurons. ME technologies are mainly designed for supraspinal structures, where the position of the neural substrate is relatively fixed to the position of the skull. The use of ME on the spinal cord and the feasibility of stable neuronal recordings involves additional challenges, mostly due to the constant movement of vertebrae during the movement. In this presentation, we will introduce the first successful neuronal recordings using ME while a nonhuman primate performed an arm-movement task and our methodological approach.

<u>2-B-14 - Rapid finger responses reflect probabilistic information about upcoming mechanical</u> perturbations

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Accurate estimates of body states are crucial to guide movements but require compensating for sensory delays. To achieve this, the brain incorporates prior information about future sensory input into feedback control signals. Here, we asked how prior information is manipulated by the brain to achieve predictive regulation of transcortical feedback loops traversing M1. In our first experiment, we assessed how prior information biases the motor output at different timescales. Participants (N=11) were instructed to quickly counter a sudden mechanical perturbation (~5 N) delivered to the ring or index finger. A visual cue anticipated the probability that either finger would receive the perturbation (i.e., 0%-100% ring-index, 25%-75%, 50%-50%, 75%-25% or 100%-0%). Beginning ~50ms post-perturbation, electromyographic (EMG) activity recorded from finger flexors/extensors (11 channels) reflected the Bayesian integration of prior information (i.e., cued probability) and sensory evidence (i.e., the stimulated finger). In line with previous work, these results suggest that transcortical loops undergo topdown regulation from upstream motor areas during response preparation. In our second experiment, we used 7T functional magnetic resonance imaging (fMRI) to assess the neural correlates of predictive regulation of finger responses to mechanical perturbations. Participants (N=6) performed the same task inside the scanner. The fMRI paradigm also included no-go trials to separate activity related to prediction and response. In no-go trials, the probability cues were presented but the perturbation never occurred. Univariate analysis revealed widespread deactivation across the primary sensorimotor cortex during response preparation. Yet, multivariate pattern analysis showed that preparation activity carried relevant information about the probability cues. In the primary somatosensory cortex (S1), the multivariate distance between conditions scaled with the cued probability difference, that is, it was larger between 0%-100% and 100%-0% (ring-index) and smaller between 25%-75%. In the premotor and primary motor cortex (M1), preparation activity mostly reflected the uncertainty of the probability cue, that is, 0%-100% and 100%-0% elicited activity patterns similar to each other but different from 50%-50%. Not unexpectedly, execution activity patterns were mostly driven by the selected finger (i.e., ring vs. index), especially in S1 and M1. In addition, unlike EMG activity, neural activity across cortical motor areas during response execution reflected the signed prediction error between the cued and stimulated finger, that is, 0%-100% and 100%-0% were more similar to each other compared to 25%-75% and 75%-25% when the stimulated finger was the one cued with a lower probability. In conclusion, these results provide new insight of how prior information is incorporated in sensorimotor responses at different levels along the motor hierarchy.

<u>2-B-15 - The modulation of corticospinal excitability and short-interval intracortical inhibition during</u> the preparation of an individualized finger motor task

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Introduction: Skilled use of the fingers is essential for daily life activities. The preparation of selective finger movements involves modulations in excitatory and inhibitory control mechanisms within the primary motor cortex (M1) that influence corticospinal activity related to finger muscles. However, fingers cannot exert movement or force completely independently; this is known as "Finger Enslaving (FE)" and is more important between adjacent fingers. The overall aim of this study was to investigate

the links between FE and the modulation of corticospinal excitability and short-latency intracortical inhibition (SICI) during the preparation of individualized resisted finger movements.

Objectives: 1) To describe the modulation of corticospinal excitability and SICI in the motor representation of the abductor digiti minimi muscle (ADM) during the preparation of individualized movements of the 2nd, 4th or 5th finger (ADM acting as a prime mover for the latter). 2) To study the association between SICI of the motor representation of the ADM and FE measured during movements of the 2nd or 4th fingers.

Methods: A selective finger force production task, with a reaction-time paradigm using visual cueing, was performed using an apparatus comprising force sensors placed under the 2nd, 4th and 5th fingers. The task could randomly involve the 2nd, 4th or 5th finger depending on the trial, while the forces produced by each finger were recorded on all trials by the force transducers. FE was calculated as : force produced by a given finger when unselected / force produced during its maximal voluntary contraction. Single and paired-pulse transcranial magnetic stimulation was used to measure corticospinal excitability and SICI of the ADM at 3 time points before movement onset. Repeated measures ANOVA were used to assess the effect of TIME and selected FINGER.

Results: Nineteen adults without major health-related conditions (9 females, 10 males; 38 ± 8.4 years old) participated. Selection of the 5th finger was associated with a significantly greater FE for the 4th than for the 2nd finger. A significant FINGER x TIME interaction was found on corticospinal excitability of the ADM. Normalized MEP amplitude increased over time during motor preparation when the 5th finger was selected (i.e., when ADM was the prime mover) as well as when the 4th finger (i.e., adjacent finger) was selected, but not when the 2nd finger was selected. No FINGER x TIME interaction was observed on SICI of the ADM, but a main effect of TIME was detected. SICI of the ADM decreased gradually during motor preparation, regardless of which finger was selected. No significant relationship was found between FE and SICI was found at the time studied.

Conclusion: Our results show that the modulation of the corticospinal excitability of the ADM during motor preparation differs according to whether the 2nd or 4th finger is selected to perform the task, although the ADM is not a prime mover for these fingers. The SICI of the ADM decreased gradually during motor preparation, regardless of the finger selected. Finally, not direct association was found between FE and SICI.

2-B-16 - Behavioral and neural constraints on motor unit control

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<u>Details</u>

The human motor system enables a vast repertoire of movements by controlling the elementary actuators of the neuromuscular system—motor units, each comprising an alpha motor neuron and the muscle fibers it innervates. However, a fundamental question remains: how does the brain coordinate the activity of spinal motor neurons to drive movement diverse behaviours that impose very different demands?

Due to the constraints posed by Henneman's size principle, neural inputs, and biomechanics, the nervous system may effectively control functional modules comprising a group of motor units. This classical framework suggests that descending neural commands may activate fixed sets of motor units

together, reducing the number of independent signals required to generate movement. However, recent findings challenge this notion, revealing violations of previously established motor unit recruitment constraints (Marshall et al. 2022, Bräcklein et al. 2022), which indicate a more flexible control. This raises a critical question: what are the principles underlying motor unit control?

We recorded the spiking activity of individual motor units using high-density surface and intramuscular electromyography (HD-EMG) in healthy human participants. Electrodes were placed on or inserted into the flexor carpi ulnaris (FCU) and first dorsal interosseous (FDI) muscles, and participants performed isometric force tasks under various conditions. In one condition (rate trial), participants tracked trapezoidal or sinusoidal profiles by modulating the discharge rate of a single motor unit. In a subsequent condition (force trial), the force exerted during the rate trial was projected for participants to track, but this time by generating force rather than controlling an individual motor unit's discharge rate. This design allowed us to compare motor unit population activity across two conditions matched for behaviour but differing in task demands—controlling a single motor unit vs using the entire motor unit pool to generate force.

Given that muscle length (and afferent feedback) is known to influence motor unit behavior, we further examined the effect of posture by rotating the wrist 90 degrees to alter the initial length of the FCU muscle and repeating both rate and force trials. By analysing motor unit activity across these conditions, we seek to determine whether motor unit control is governed by fixed modules or exhibits greater flexibility.

Our findings will shed light on a fundamental question in systems neuroscience: how the central nervous system orchestrates motor unit activity to generate movement. Understanding these principles may provide crucial insights into neuromuscular function and rehabilitation strategies for motor impairments.

<u>2-B-17 - Egocentric gaze and allocentric background reference frames are integrated to represent and express motor memory</u>

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How the brain integrates motor memories represented in different reference frames is an open question in motor control neuroscience. Past research has shown that motor memories are represented in a mixture of intrinsic body-based (joint angles) and extrinsic world-based (cartesian x-y axes) coordinates (Braianov 2012). However, many possible extrinsic frames could represent the same movement, such as gaze, head, or world-centered (Andersen 1997). It is still unclear whether each extrinsic frame is used and how they are integrated to shape motor memory. Here, we present the results of our four experiments (n=152 in total), suggesting that gaze and background (but not head) reference frames are integrated to represent and express motor memories and that conflicting motor memories, which normally cause interference in learning, can be learned faster if they are represented differently in those reference frames.

In our experiments, participants performed a reaching task to a single target in a training workspace, while a visuomotor rotation was gradually introduced up to 30°. Learning generalization was tested on 13 untrained targets in a different workspace since the generalization pattern (function) reflects how the brain represents the learned movement (Shadmehr 2004).

First, we manipulated the orientation of the gaze (Exp-1: n=48), head (Exp-2: n=16), and rectangular visual background (Exp-3: n=16) and examined its effects on generalization. Our results showed significant peak shifts of the generalization function towards the gaze and visual background orientations (p < 0.001 for both) but no significant peak shifts towards the head orientation (p = 0.98). These results suggested that the gaze and background frames were integrated to shape motor memory. Consistent with our Exp-1 (gaze) results, a recent study (Abekawa et al., 2022) has shown that conflicting motor memories for arm reaching can be simultaneously learned by changing gaze location. A similar thing may be observed if there is a background-specific motor memory. To examine this possibility, we examined an interference effect of two opposing visuomotor rotations (Exp-4: n=72), each associated with different visual background orientations while controlling the gaze orientation. Our results showed that, after adapting to a visuomotor rotation with a specific background orientation, another opposing visuomotor rotation can be learned faster if the background is displayed in a different orientation (p < 0.001).

Together, our findings suggest that the egocentric gaze and allocentric background reference frame are integrated to represent and express motor memories and that interference between conflicting motor memories can be mitigated if their memory representations are not aligned in such an extrinsic reference frame.

2-B-18 - Encoding of muscle synergies by interneuronal populations in the spinal cord

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<u>Details</u>

The central nervous system controls movement through neuromotor modules known as muscle synergies. Previous studies suggest that spinal premotor interneurons contribute to the encoding of muscle synergies during voluntary movement in monkeys. However, motor output is also shaped by descending and sensory inputs, which may configure spinal interneuronal networks into different sets of muscle synergies under varying spinal states. Despite these insights, how synergies are encoded by spinal interneurons remains unclear and less is known about the specific interneuronal subtypes involved in synergy organization.

To address these questions, we employed optogenetics to selectively stimulate excitatory spinal interneurons in anesthetized Thy1-ChR2 transgenic mice while simultaneously recording intramuscular electromyographic (EMG) activities and spinal interneuron spikes. Neural activities were recorded using 64-channel silicon probe electrodes (H10, Cambridge Neurotech). To achieve comprehensive stimulation of the lumbosacral spinal cord, we incrementally moved the laser in 200-µm steps along the exposed spinal surface. Using spike-triggered averages of EMGs, the post-spike effects on the recorded muscles were measured as muscle fields. The muscle field reflects the connectivity strength of the recorded unit to the muscles.

Our findings reveal that the muscle fields of interneurons upstream of premotor interneurons closely align with muscle synergies extracted from EMG signals using non-negative matrix factorization (NNMF). However, the firing rates of these units, despite their muscle fields matching the synergies, do not correlate with the corresponding synergy activities. Additionally, we observed that the muscle fields of individual spinal interneurons changed under different stimulation conditions. These results suggest that each muscle synergy may not be represented just by individual spinal interneurons. To further investigate synergy representation, we applied least squares regression to approximate muscle synergies using multiple muscle fields from different units. We found that both muscle synergies and their activities could be effectively reconstructed by a population of interneurons. Notably, we identified a subset of units with overlapping synergy membership across different stimulation conditions that consistently encoded the same muscle synergies.

These findings suggest that muscle synergies may not be controlled by isolated upstream spinal interneurons but are instead represented by spinal interneuron populations. We argue that during locomotion, spinal interneuronal ensembles are dynamically coordinated to shape the muscle synergies, allowing for flexible motor control across different spinal states.

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2-B-19 - Motor working memory & mental rotation

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<u>Details</u>

Shepard and Metzler's groundbreaking 1971 study revealed a striking pattern: the greater the rotation between two 3D objects, the longer it took participants to determine if they were identical. This finding suggested that mental rotation mirrors physical rotation (Shepard & Metzler, 1971). Since then, substantial research has been conducted to better understand the cognitive processes supporting mental rotation. There is evidence that the mental rotation and visual working memory share a common neural substrate (Anguera et al., 2010; Suchan et al., 2006), however it is unclear if mental rotation is a direct function of visual working memory (Beschin et al., 2005; Ebert et al., 2024; Hyun & Luck, 2007). The relationship between mental rotation and WM has been primarily explored in the context of visual WM, however mental imagery is not strictly dependent on visual imagery (Marmor & Zaback, 1976). Therefore, we sought to investigate the relationship between mental rotation and non-visual motor WM.

Motor WM has been found to encode movement information through both effector-specific (limbdependent) and effector-independent (abstract) representations (Hillman et al., 2024). To examine how mental rotation influences motor WM, we conducted a dual-task interference study. Participants first encoded a passively guided reaching movement. While maintaining this movement in working memory, they completed a Shepard & Metzler-style mental rotation task. Afterward, they were prompted to recall the reaching movement using either the same or opposite arm. Since recall with the opposite hand can only rely on effector-independent information we were able to dissociate between effectorspecific and effector-independent motor WM representations.

Our results indicate that increasing the angle of rotation in the mental rotation task leads to greater angular error in the motor working memory (WM) task—but only when participants switched hands.

This suggests that effector-independent motor WM is selectively disrupted by mental rotation, with the degree of interference scaling with the magnitude of the preceding rotation.

2-B-20 - Chronic stability of human motor manifolds that enable iBCI cursor control

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Details

Intracortical brain-computer interfaces (iBCIs) allow people with paralysis to control peripheral devices with motor cortex activity, offering a promising avenue for functional compensation of motor deficits. Despite a large body of work in animal models demonstrating the benefit of studying low-dimensional neural representations in motor control ("neural manifolds"), human motor cortex manifolds remain poorly characterized. In particular, because iBCI decoders are typically recalibrated daily, it is unclear whether there is a stable low-dimensional structure that could be utilized by the decoder, as has been suggested in non-human primate work (Gallego et al., 2020). The goal of this study was to characterize the long-term stability of a human motor manifold for iBCI control. Data were collected from three people with tetraplegia who were enrolled in a clinical trial of an iBCI conducted under an FDA Investigational Device Exemption (NCT01894802). Each had two 10x10 intracortical microelectrode arrays implanted in motor cortex (Blackrock Microsystems, Inc.). Participants used their iBCI to complete a center-out cursor control task over an extended period of time (P2: n = 83 sessions across 911 days; P3: n = 27 sessions across 804 days; P4: 52 sessions across 536 days). Neural data recorded during iBCI calibration from each session were aligned into a common low-dimensional space using generalized Procrustes alignment (GPA) for each participant. Firing rate data was first projected into a lowdimensional space using factor analysis and, for each day, a trial-averaged manifold was created consisting of low-dimensional neural trajectories for each center-out target. A 'template' manifold was calculated as the shape that maintained minimal distance from all other daily manifolds. Neural data from each session was aligned to this template. Neural representations measured each day aligned well to the template manifold (average correlation: 0.75 ± 0.10 P2, 0.79 ± 0.10 P3, 0.78 ± 0.12 P4), suggesting this method identified a latent structure involved with iBCl control. To test whether the latent neural manifold remained stable over time or drifted with increasing distance in time, pairwise correlations between daily manifolds were organized by the gap in days between their respective sessions. Manifold pairs were correlated with one another (Pearson correlation = 0.66 ± 0.05 std P2; 0.70 ± 0.05 P3; $0.75 \pm$ 0.05 P4) and the relationship was stable over time (weighted least squares (WLS) slope magnitude < 1e-4, R^2 magnitude < 0.1 for all participants. p > 0.1 for P2 and P4 but p < 0.05 for P3, suggesting poor model fit given small slope and R². WLS weighted by number of comparisons at each day gap). These data show that despite day-to-day changes in recording stability, daily decoder recalibration, and other factors, we observe a stable low-dimensional representation that is involved in iBCI control in humans for many months to years.

<u>2-B-21 - Does cognitive load affect movement preparation and coordination differently based on side</u> <u>of brain damage?</u>

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More than 75% of stroke survivors deal with some form of upper limb impairment, which affects the guality of movement they produce. Since movement involves a combination of intact cognitive, sensory, and motor execution processes, a deficit in any of these can affect functional outcomes. While the lateralization of motor and sensory processes has been extensively studied (Sainburg, 2002; Rogers, 2000; Goble et al., 2006), literature on the lateralization of cognitive processes related to movement provides mixed results. Some studies describe a right hemisphere specialization for movement preparation and spatial working memory, while others also suggest a left hemisphere specialization for verbal working memory (Schaefer et al., 2012; Philipose et al., 2007; Andrews et al., 2014). We examined the cognitive-motor interaction by studying whether cognitive aspects of movement, such as working memory and action selection, were lateralized, and if so, how they would affect functional outcomes in stroke survivors with left or right brain damage. We hypothesized that with increased cognitive load (i.e., the total effort imposed on working memory during a movement), movement preparation and muscle coordination would differ based on side of brain damage. Previous studies have shown that with increased cognitive demands, there may be asymmetries in muscle activity related to postural control. We developed a cognitively challenging reaching task on the Kinereach system where participants had to commit pictorial cues to memory in order to locate and reach for the correct object within 3 s. The level of cognitive load on the participant increased over the course of the task. We recruited 15 chronic stroke survivors with severe hemiparesis for this study (7 females; 8 males; age 58 years +/- 3.09 SEM; 9 right brain damage, 6 left brain damage). We collected position and orientation information of the ipsilesional arm using electromagnetic sensors placed on the hand and upper arm. We also recorded EMG activity from the posterior deltoid, pectoralis, biceps, and triceps muscles. Since our participants did not have functional use of their contralesional arm and because motor deficits exist in the ipsilesional arm as well, we examined deficits in cognitive aspects of movement in the ipsilesional arm only. We found that reaction time increased with the level of cognitive load (p < 0.0001); however, no group differences were found. We also found that individuals with right brain damage produced less spatially efficient trajectories compared to those with left brain damage (p = 0.01), suggesting a potential role of cognitive load in reversing the dynamic dominance model prediction of less spatially efficient trajectories with left, not right, brain damage. Our ongoing analysis of the EMG data suggests that joint cocontraction does not change considerably with increased cognitive load, which is not supportive of our hypothesis. These preliminary results suggest that while movement preparation is impaired with increased cognitive load, this may not be at the cost of differing muscle coordination patterns.

2-B-22 - Cerebellar control of context-dependent motor timing

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<u>Details</u>

Organisms often rely on environmental context to guide the timing of actions. Whether evading a predator, avoiding a vehicle, or timing a sidestep to dodge an opponent, context provides crucial information to ensure effective actions. Here, we study the role of cerebellar circuitry in context-dependent motor timing tasks by linking feedback from a manual response task to a periocular airpuff, a stimulus commonly used in Pavlovian eyeblink conditioning to elicit learned motor responses. Rodents are presented with either a dark or light tunnel as an environmental context that signals the expected time at which a lever can be pulled. If the lever is not pulled within a designated temporal window, a

periocular airpuff is administered as punitive feedback to facilitate learning of the expected response time. We found that rodents learned to adjust their response timing based on environmental context. In some cases, we observed well-timed, context-dependent conditioned eyeblink responses. To investigate the neural basis of this behavior, we performed extracellular recordings from cerebellar lobule IV/V and Simplex. We found that cerebellar Purkinje cells and other cortical neurons exhibited context-dependent signaling that followed the behavioral patterns of the animals. To further explore these findings, we developed a computational model explaining how cerebellar circuitry could perform context-dependent computations that could lead to well-timed control of manual and conditioned eyeblink responses. These findings suggest that cerebellar cortical neurons could play a role in contextual control of motor timing responses across different effectors.

2-B-23 - Action planning and execution under sensory uncertainty in younger and older adults

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<u>Details</u>

Humans often plan and initiate an action before having full certainty about its outcome. For example, when returning a spinning tennis shot, a player must decide on a trajectory before knowing whether the ball will curve left or right. In laboratory-based tasks, when people face similar uncertainty about which goal to pursue, they frequently generate movements that are intermediate between the potential goal locations. This has been studied using "go before you know" reach-to-target paradigms, in which participants are required to initiate a movement toward one of two potential targets without knowing in advance which will be correct. The true target location is only revealed after movement onset, reliably eliciting intermediate movements. Critically, the extent to which intermediate reaches under heightened uncertainty are implemented depends on their relative advantage - occurring more often with sufficient time for online correction and when competing target locations are close together. In this study we determined how age modulates motor planning under conditions of heightened sensory uncertainty, with the hypothesis that age-associated sensory and motor declines would limit rapid online corrections necessary for intermediate reach movements. We compared kinematic outcomes measures in younger (n = 15) and older adults (n = 12) using a "go before you know" reach-to-target paradigm. To manipulate sensory certainty, participants received sensory probability cues indicating either high (80%) or low (50%) probability of reach direction. Preliminary results showed fewer intermediate reaches in older than younger adults. These results suggest that older adults might preferentially rely on rigid feedforward than online control strategies as a compensatory mechanism for known sensorimotor declines.

<u>2-B-24 - Effects of orally administered Deschloroclozapine on fine hand movements in Rhesus</u> <u>Macaques</u>

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Details

Chemogenetic studies frequently employ deschloroclozapine (DCZ), a ligand that demonstrates potency in inhibiting neurons that express DREADDs (Designer Receptor Exclusively Activated by Designer Drugs). These studies have become foundational in understanding the function of specific neuronal populations in vivo. However, despite the widespread use of DCZ, its baseline effects on motor function independent of DREADDs activation remain poorly characterized. The lack of detailed knowledge about DCZ's direct impact on motor behavior poses a challenge in accurately interpreting experimental results.

This study aimed to address this gap by examining the impact of orally administered DCZ on fine motor control in rhesus macaques (n = 2) during a touch panel reaching task, focusing on index and middle finger movements. Subjects received oral DCZ at doses of 0.0 mg/kg (baseline), 0.1 and 0.3 mg/kg. Video pose estimation analysis revealed dose-dependent alterations in movement velocity and smoothness. Index finger movements showed pronounced changes, with mean velocity increasing by 2.56% at 0.1 mg/kg and 26.20% at 0.3 mg/kg relative to baseline (p < 0.001), accompanied by parallel changes in peak velocity (p < 0.001). Middle finger responses were more variable, with significant effects emerging only at 0.3 mg/kg for both mean velocity (p = 0.004) and peak velocity (p = 0.010).

Interestingly, higher DCZ doses were associated with reduced movement smoothness, with significant effects observed at 0.3 mg/kg for both index and middle fingers (both p < 0.001). This suggests a marker of motor control degradation, and may indicate a disruption in the fine-tuned coordination of muscle movements. Yet, the 0.1 mg/kg dose showed no significant effects on movement parameters (all p > 0.4), suggesting a dose threshold for motor effects. Notably, task motivation and performance accuracy remained unchanged across all conditions, indicating that the observed motor changes were not due to a lack of engagement or an overall decline in cognitive performance.

While the small sample size limits broader generalization, these findings provide a preliminary indication that DCZ influences fine motor control in a dose-dependent manner, warranting further investigation through more extensive testing in these and additional subjects, even without DREADD expression. The differential effects between digits suggest that task-specific impacts may modulate DCZ's motor effects, potentially through interactions with specific neurotransmitter systems or receptor subtypes, which require further exploration. These results underscore the importance of considering DCZ's baseline effects when interpreting DREADD studies and call for investigation with larger cohorts and expanded dosage ranges to fully characterize its motor impacts in primates. Such efforts will be crucial in guiding the design of more reliable chemogenetic experiments.

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2-B-25 - Posture affects limb preference during reaching in primates

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Details

Primates, like many animals, interact with the environment using their forelimbs. Some actions, such as peeling a banana, require both limbs; but many actions require only one limb and often either limb is sufficient. In these cases, the animal chooses which limb to use. Studies in humans reveal a general ipsilateral limb preference - favoring the left limb for left-side targets and the right limb for right-side targets - and demonstrate key factors such as task demands, movement efficiency, and biomechanical

constraints that alter this preference, but the neural mechanisms governing limb selection remain poorly understood.

A non-human primate model allows for both behavioral analysis and direct investigation of neural mechanisms. To address the validity of this model, we trained two non-human primates (*Macaca mulatta*) to reach for stimuli on a touch screen. Before each reach, the subject fixated a central point while placing each forelimb's hand on a "home" button positioned 20 cm in front of the subject at waist level. The reach target then appeared at a random position on the screen and the subject reached for it with one limb to receive a liquid reward. The non-reaching limb remained on its home button while fixation and the reaching limb were free to move.

As expected, subjects exhibited an ipsilateral limb preference, with a point of reach equality (PRE) near midline. Reaches across the PRE with the "less preferred" limb were associated with longer reaction times, suggesting a deliberative process.

We examined which parameters influence limb preference by testing three manipulations of starting posture: 1) home button positions, 2) eye fixation position, and 3) head yaw. All three manipulations shifted the subject's PRE in the same direction as the postural change, suggesting that limb selection is influenced by the body's orientation. Surprisingly, head yaw had the largest effect, approximately twice that of the home button and fixation shifts. These data suggest that limb selection is influenced by multiple cues, with head orientation playing a particularly strong role. Furthermore, manipulations of limb preference will be critical for probing the neural mechanisms underlying limb selection in future studies.

2-B-26 - Corticostriatal contributions to skilled motor actions and trial and error learning

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<u>Details</u>

Motor cortex (M1) and striatum work together to plan movements, potentially through the generation of motor commands and the kinematic control of performance respectively (Dudman and Krakauer, 2016). This hypothesis has clear and testable predictions about the contribution of M1 to striatal dynamics and the production and modification of behavior. Here we seek to understand how these brain areas work together to generate skilled motor actions and how these motor commands can be modified when task requirements change.

First, cohorts of mice were trained to move a joystick past a learned threshold . Upon reaching expert performance, M1 was bilaterally lesioned. Starting on the day of the lesion, behavior and striatal activity were assayed for 20 days. We found that M1 was required for skilled reaching as animals were largely unable to perform the task for 8-10 days post lesion. In what reaching behavior we did see post lesion, striatal activity was absent, suggesting striatum was not responsible for the selection of the action to perform. We found that following lesions , reach kinematics were altered to allow for recovery of behavior after 10 days post lesion. Reach-related striatal activity began to appear as the behavior

recovered; however, the observed neural dynamics no longer encoded movement kinematics and could not be used to predict movement trajectories. These data suggest that M1 is required for skilled reaching and in its absence, striatum alone cannot produce these goal-directed behaviors. Additionally, we found that following lesions, mice were able to groom and locomote normally, however they displayed profound freezing of gait like behavior when needing to decide to turn right or left in an unrewarded maze, suggesting M1's role in the updating of motor state.

We next sought to assay how population activity of M1 and striatum can facilitate trial and error learning and modify motor commands. We trained a separate cohort of mice to reach within a limited range of amplitude and importantly, mice only were instructed as to trial success or failure. In a subset of sessions, the learned target amplitude was shifted mid-session and mice had to modify their behavior based on reward feedback alone. Using concurrent M1 and striatal recordings, we found that upon moving the target, encoding of joystick amplitude was maximal in layer 5 (L5) and dorsal striatum while there was an increase in encoding of trial outcome, following reward delivery in both striatum and superficial cortex (L2/3). We also found that encoding of previous trial outcome peaked in ventral striatum prior to reach onset. These findings suggest that upon recognizing a change in task demands, neural populations of the striatum in tandem with neurons of L2/3 orchestrates the appropriate update to motor performance and these actions are carried out by L5 and dorsal striatum on subsequent trials.

<u>2-B-27 - Spatial gradient of population representations about hand and eye positions in macaque</u> <u>motor cortex</u>

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Details

Recently, population analyses provide new insight into how neurons implement flexible computations to guide movement. For instance, different types of information can coexist in a single cortical area while being separate (orthogonal) at the level of population representations (Sun et al. 2022). The dorsal premotor cortex (PMd) is thought to integrate information from multiple effectors, encoding eye and hand positions, when studied at the level of single neurons (Pesaran et al. 2006). However, population representations of eye and hand positions, and their distribution across frontal motor cortices remain unclear. Population analyses in spatially localized areas may provide new insights on underlying computation involving different effectors. We therefore investigated population representations in multiple effectors using a high density laminar probe to sample neural activity at different locations in PMd and the primary motor cortex (M1). We trained one male macague monkey to perform a saccade task with three different hand positions to investigate representations of each effector. The monkey had to fixate an initial eye target and maintain the hand position during the delay period (400 ms - 700 ms). He then had to generate a saccade to an eye target while maintaining his hand position. We recorded single-unit activity using a Neuropixels targeted to PMd or M1(4 sites, N=82, 132, 55, 46 neurons). We analyzed firing rates in the delay period across 27 conditions (three hand positions, three initial eye targets, and three eye targets). We quantified information about each target at both the single-unit and population level using linear discriminant decoding analysis and principal component analysis. Our results showed that neurons that encoded initial eye targets, hand positions, or eye targets were present in all recording sites, but the amount of eye related information and the number of eye encoding neurons tended to increase in more rostral areas. Population analyses revealed that hand related information was isolated from information about initial eye positions in M1, but less isolated in

more rostral sites. This suggests underlying computation involving eye and hand positions varies across areas. We then built a recurrent neural network (RNN) with three modules to explore network structures that could give rise to a gradient of effector information and orthogonal population representations. In the simulation, the first module receives target stimulus and outputs eye positions, a M1 module outputs hand positions, and a PMd module bridges between the two modules. The network was trained using eye and hand positions from experiments. The network reproduced orthogonal representations in M1. This isolation may be required to minimize the influence of eye movement on hand positions. Our study highlights the importance of spatial mapping and population analysis in motor areas.

<u>2-B-28 - Neural dynamics underlying behavior are preserved across species in an evolutionarily-</u> <u>conserved brain region</u>

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Details

Over evolutionary timescales, natural selection guides changes in ancestral brain circuits to produce behaviors that are advantageously adapted to each species' environment. Nevertheless, aspects of the resulting neural circuitry, such as anatomical features of brain regions, are conserved across distinct species with distant evolutionary origins such as rodents and primates. However, it remains unclear whether these ancestral regions perform similar functional computations in divergent species. Here, we hypothesized that despite their phylogenetic distance, mice and monkeys should have highly preserved neural population dynamics while performing similar behaviors, indicative of evolutionarily-preserved computational principles. We trained both mice and macaque monkeys to produce skilled movements using their forelimbs. We recorded spiking activity from populations of neurons in the motor cortex—a region prevalent throughout higher vertebrates whose activity is tightly linked to and necessary for skilled movement—of individuals of both species as they performed highly similar reaching and grasping behaviors. We directly compared the geometric and dynamical similarity of neural population activity across these species using canonical correlation analysis (CCA) and dynamical similarity analysis (DSA), respectively. Surprisingly, we found that both geometric and dynamical features of neural dynamics were highly preserved across species despite millions of years of divergent evolution. The neural dynamics across species performing the same behavior were more preserved than those within individual monkeys between different behaviors. Importantly, we found that the geometry of neural population trajectories changed proportionally to behavioral differences, but not the underlying dynamics. Using recurrent neural network modeling, we demonstrate that geometric and dynamical signatures of neural population activity can be predictably and reliably dissociated by manipulating architectural properties and learning rules, reinforcing that the preservation observed in biological brains is an intriguing and unexpected phenomenon. Our results thus demonstrate strong preservation of neural computational principles across species. We posit that evolution has identified stable computational principles that provide a fundamental basis for behavior in multiple species.

2-B-29 - Continuous visual feedback increases the accuracy of our self-attribution of action outcomes Christoph Schneider ¹, Raz Leib ², David Franklin ², Mathias Hegele ³, Johannes Keyser ⁴

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<u>Details</u>

Our sense of agency, which refers to the attribution of an action and its outcome to oneself versus external causes such as other agents, is a crucial prerequisite for successfully interacting with an everchanging environment. It relies on predictions about the sensory consequences of our own actions based on the efference copy, reafference and forward models. These mechanisms help us distinguish self-generated sensory signals from those sensory signals that are triggered by external sources.

The formation of the sense of agency was previously proposed as a Bayesian observer model in which sensory observations of oneself and other agents are quantified as likelihoods. According to this model, the self-likelihood is largely determined by comparing sensory predictions and outcomes. If this hypothesis were correct, we would expect that the amount of information provided by sensory input to the agent would modulate the process of determining self-agency. Specifically, increasing the availability of sensory feedback during a self-generated action should improve the ability to distinguish one's own actions from those of another agent. We sought to test this model prediction by manipulating the extent of visual feedback.

Participants (n = 25) performed goal-directed movements to hit a puck and propel it toward a target. Within this virtual air hockey game, an unseen second agent perturbed the players' actions to create an alternative to one's own contribution of the action outcome. The pucks' trajectory was randomly either shown continuously or omitted on a trial-by-trial basis. In different phases of the experiment, participants were further asked to hit specific targets, predict their or the other agents' outcomes, or provide judgments of self-attribution about the action outcome.

Our data show that the visibility of the puck trajectory significantly improved the accuracy of predicting its final position ($M = 1.61^{\circ}$, $SD = 0.53^{\circ}$) compared to trials with omitted trajectory ($M = 6.81^{\circ}$, $SD = 2.10^{\circ}$). We additionally found that the amount of sensory feedback substantially modulated the sense of agency. In the absence of perturbations by the other agent, participants claimed agency over their actions. Yet, in the presence of the other agent who could have perturbed the puck's trajectory, and thus influenced the action outcome, the probability of self-attribution by the players decreased significantly when continuous visual feedback was available. This is exhibited as shift in the point of subjective equality in trials with visible trajectory ($M = 4.36^{\circ}$, $SD = 2.26^{\circ}$) versus a mean of 9.54° ($SD = 3.83^{\circ}$) for trials without trajectory information.

These results suggest that additional sensory feedback changed the self-likelihood function and, crucially, increased the accuracy of self-attribution. Our results thus provide further evidence for the Bayesian observer model as an effective conceptual framework for elucidating the mechanisms underlying the sense of agency.

2-B-30 - Motor cortical signals shared between finger movements are related to wrist stabilization

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<u>Details</u>

Human manual dexterity is enabled by the intricate anatomy of the hand – comprised of muscles spanning many wrist and finger joints at the same time – and complex neural activity of the motor

cortex (MC) that controls these muscles. However, it remains an open question whether the motor cortex encodes hand movements through a framework of postures or muscle-related control signals. In this study, we investigated the cortical representation of human hand movements, leveraging a clinical trial that involves five participants with impaired hand function who were implanted with electrode arrays in the MC. This allowed us to map the extensive space of hand postures available to humans, ranging from isolated single-digit movements to coordinated movements of the fingers and wrist. Participants were first instructed to imagine flexion and extension of individual digits. Neural activity in the MC enabled accurate decoding of both the digit being moved and its movement direction. To identify the shared neural patterns underlying flexion and extension of different digits, we trained five decoders to predict the movement direction of the thumb, index, middle, ring, or pinky finger. When these decoders were applied to predict movements of other digits, their performance dropped, as expected. However, training a model with a dataset containing movements of all digits rescued the performance, suggesting a shared representation of finger flexion and extension across digits. This shared representation likely reflects the activation of wrist-stabilizing muscles, which behave similarly during movements of all fingers.

To directly investigate the nature of this shared activity, participants were asked to imagine moving their wrist to five wrist postures in combination with, and separately from, the finger movements. Contrary to our expectations, neural signals for the fingers and wrist could be linearly separated during simultaneous movements. However, a decoder trained on trials that contained only wrist movements generated consistent wrist movement predictions for a given digit, although the predictions varied with digit and movement direction. This pattern aligns with the expected behavior of muscles stabilizing the wrist during finger actions.

These findings suggest a muscle-based organization of motor cortex activity, where movement-related signals of individual digits and wrist joints contain information about the recruitment of muscles spanning other joints. Leveraging this insight, we developed motor intent decoders that enabled participants to control the fingers and wrist of a virtual hand with high accuracy. These results elucidate a framework for understanding the neural representation of the hand in the motor cortex and lay the groundwork for developing more dexterous and intuitive brain-computer interfaces.

2-B-31 - Structured representation of a symbolic action grammar across primate frontal cortex

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<u>Details</u>

At the core of cognition is proficiency in solving new problems. This depends on goal-directed generation of novel thoughts and behaviors (compositional generalization), which is widely thought to rely on internal representations of discrete, abstract units, or "symbols", and syntactic rules that recombine symbols into a very large set of possible complex representations. Combined, symbols and syntactic rules constitute the two components in an internal "grammar" for systematically generating representations. Although this view has been highly influential in formulating cognitive-level explanations of behavior, the neural substrates of symbols and syntax remain unclear.

To elucidate the neural basis of symbolic representations, we established a task paradigm for testing compositional generalization—an ability thought to depend on symbolic representations—in macaque monkeys. This task capitalizes on the brain's remarkable ability to generate novel, goal-directed actions,

an ability which has been hypothesized to depend on symbolic representations, in which discrete, abstract units of action (action symbols) are recombined. Action symbols may be especially important for novel, complex sequences, such as in the imitation of a new dance by internally composing action symbols representing discrete types of dance pose.

Here, we identify a neural representation of action symbols localized to a specific area of frontal cortex. In monkeys performing a drawing task designed to assess recombination of learned action symbols, we find behavioral evidence for three critical features that indicate actions have an underlying symbolic representation: (i) invariance over low-level motor parameters (location and size), (ii) categorical structure reflecting discrete types of action, and (iii) recombination into novel sequences. In simultaneous large-scale neuronal recordings across motor, premotor, and prefrontal cortical areas, we find that population activity in ventral premotor cortex (PMv/F5), and no other recorded area, encodes planned actions in a manner that, like behavior, exhibits motor invariance, categorical structure, and recombination. These findings reveal a neural representation of action symbols in PMv, and thus identify a putative neural basis for symbolic operations in the generation of novel actions.

In ongoing work, we are investigating the neural basis of syntactic operations, the second of the two components (along with action symbols) that constitute putative internal action grammars. We find initial evidence for a representation of syntax in specific areas of prefrontal cortex.

These findings (i) establish a task paradigm involving symbolic abstraction in motor behavior, (ii) identify a neural representation of action symbols in PMv, and (iii) give initial insights into the neural representation of syntax. These are foundational steps towards elucidating the mechanisms of symbolic operations in an internal action grammar.

<u>2-B-32 - Algorithmic and retrieval strategies have differential impacts on implicit recalibration in a visuomotor adaptation task</u>

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<u>Details</u>

The dynamical systems perspective proposes that cortical preparatory activity seeds the temporal evolution for generating movement. To intercept a moving object, the brain must adapt the internal body states to the external world to compensate for pervasive sensorimotor delays. Our recent studies showed that pre-movement activity in sensorimotor cortex takes into account these delays. However, the exact mechanism by which this preparatory process unfolds remains unclear. The long-standing Tau theory posits that a simple variable, time-to-contact (Tau), could guide interception. Here, we investigate whether such a variable – continuity of both inner states and external cues - is embodied in cortical preparatory activity for successful interception. We trained two rhesus monkeys on delayed reach directed at static or moving objects. Moving targets followed a circular path at four velocities (clockwise/counterclockwise, 95/190 deg/s). The delay duration was randomized, and trial conditions alternated, making the final target location pending. Single-neuron activity from the primary motor cortex and premotor cortex was recorded using Utah arrays (n > 60 per monkey). PCA identified a conserved preparatory subspace shared by both static and moving conditions, with prep-PCs stable in the static condition but continuously updated in the moving condition. Based on subspace alignment, we identified a 2-D auxiliary subspace where prep-PCs matched target angular coordinates in the static condition. In the moving condition, neural angular features led target directions, suggesting continuous

prediction of the moving target. Cross-correlation metrics showed a peak, consistent across target velocities, aligning with reaction and movement times. This suggests that the Tau is embodied in preparatory activity, enabling interception ready for a random trigger. To explore the mechanism underlying the continuous updating of preparatory activity, we introduced two task variants. First, we trained monkeys to learn an interception with target occlusion. The moving target disappeared 400 ms after target onset for 400 ms. During the occlusion, prep-PCs continued updating, indicating that the Tau, once formed, might continue to guide movement even in a brief absence of sensory input. Second, we trained monkeys on an interception task with target jumps. The moving target jumped forward by 81° at 400 ms after target onset. We observed significant changes in prep-PCs following the target jump, with a marked increase in neural distance from the standard interception. The minimal differences showed in prep-PCs when aligning to the same reaching direction, indicating that the brain can rapidly adapt Tau to a changing environment, enabling corrected predictions. Overall, these findings provide direct neural evidence that time-to-contact is continuously embodied in cortical preparatory activity for flexible interception in dynamic and unpredictable conditions.

2-B-34 - Eliminating interlimb transfer asymmetry in motor skill learning

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Details

Motor skill learning is more effective when it transfers to untrained contexts, especially in sports training and motor rehabilitation. The phenomenon of interlimb transfer refers to the improvement in performance of both the trained and untrained contralateral limbs following unilateral motor practice. However, in many cases, interlimb transfer occurs asymmetrically, with varying degrees of transfer between the limbs. The reasons for this asymmetry remain unclear. This study aimed to investigate whether motor skill learning could transfer between limbs, whether this transfer occurs asymmetrically, and how such asymmetry can be eliminated.

Two experiments examined interlimb transfer in motor skill learning using a laser pistol shooting task. In Experiment 1, two groups of right-handed participants practiced shooting with either their dominant hand (DA) or nondominant hand (NA) during the acquisition phase. Performance was assessed before training, immediately after training, and one day post-training, using both hands in a randomized order. The results showed that shooting skill transferred from the dominant to the nondominant hand in the immediate posttest, but not vice versa. However, transfer from the nondominant to the dominant hand was observed on Day 2. We speculate that although skill transfer from the nondominant to dominant hand is possible, the expression of this transfer in the dominant hand was inhibited immediately after training.

In Experiment 2, we tested whether activation of the dominant hand, following nondominant-hand training, could be facilitated through unrelated motor tasks. Participants were divided into three groups, each of which learned the shooting skill with their nondominant hand. Two activation groups then engaged in either a fine mouse tracking task (NA + Tracking) or a gross typing task (NA + Typing) using their dominant hand, while another group rested their hands by watching a video, which served as the control (NA + Rest). Pretest and posttest measures were taken for both hands in a randomized order before and after the acquisition and activation phases. The results showed that the NA + Tracking group exhibited dominant-hand performance comparable to that of the DA group on Day 1, and superior performance compared to the other left-hand acquisition groups (NA, NA + Typing, NA + Rest).

The findings reveal that interlimb transfer of shooting skill is asymmetric: transfer from the dominant to the nondominant hand is larger than the reverse. However, the asymmetry can be eliminated by activating the dominant hand with a fine motor task after nondominant-hand acquisition. These results suggest that interlimb transfer can be fully facilitated by removing possible inhibitory effects from the nondominant hemisphere to the dominant hemisphere. Our findings challenge existing models of interlimb transfer and have important implications for practical applications in motor skill training and rehabilitation.

C – Posture and Gait

2-C-36 - Does the interplay of postural constraints and reward probability influence movement vigor?

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<u>Details</u>

Background

While reward probability is well known to enhance the vigor of focal movements (e.g., increased velocities and shorter reaction times), its influence under postural constraints remains poorly understood. Anticipatory Postural Adjustments (APAs) are crucial for maintaining stability, as they counteract destabilizing forces before and during goal-directed actions. Since APAs are integral to movement execution under postural constraints, investigating how reward probability modulates APAs can provide critical insights into how the nervous system balances reward-driven motor adjustments with postural stability. This study aimed to examine how reward probability influences APAs and movement vigor under postural constraints, offering a deeper understanding of reward-based motor control.

Methods

Twenty-four participants performed a bimanual task, moving a shared manipulandum forward or backward on a table. Visual feedback provided real-time guidance. Each participant completed 48 trials per movement direction under four reward-probability conditions: 0%, 17%, 83%, and 100%. Higher-probability blocks offered more frequent point-based incentives. We measured Reaction Time (cue to movement start), Premotor Time (cue to APA onset), APA Time (APA onset to movement start), APA Amplitude, and movement kinematics (peak velocity, movement time, and overshoot).

Results

Higher reward probability led to shorter reaction times and increased peak velocities, replicating known effects on movement vigor. However, this came at the cost of reduced precision (greater target overshoot), reflecting a well-established speed-accuracy trade-off. Regarding postural adjustments, increased reward probability was associated with earlier APA onset (shorter premotor time), while APA duration often remained unchanged. These effects were observed in both movement directions, though with varying magnitudes. Task completion time also decreased with greater reward likelihood, suggesting that participants prepared their postural strategy more quickly when incentives were higher.

Importantly, these reward-driven APA changes did not compromise postural stability, indicating a coordinated, incentive-sensitive mechanism optimizing both posture and movement.

Conclusion

Our findings demonstrate that reward probability shapes not only primary movement vigor but also postural preparation. Higher incentives drive earlier and more robust APAs, reflecting a broad motivational influence across the motor system. These insights expand current models of reward-based motor control by emphasizing the role of postural adjustments. Understanding how reward modulates APAs may have implications for training and rehabilitation, where motivational factors could enhance both stability and movement efficiency.

2-C-37 - Cortico-basal ganglia dynamics underlying sensorimotor integration during skilled locomotion

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Details

Locomotion is a fundamental behavior exhibited by all vertebrates across the animal kingdom. Despite seeming like an automatic behavior, locomotion requires the coordinated activation of muscles through spinal circuits (central pattern generators; CPGs) which are partly driven by supraspinal inputs. While electrophysiological and neuroanatomical studies of the CPGs have revealed a clear organization that explains different forms of locomotion, it is not clear how their activity is modulated by supraspinal inputs. Cortical areas such as PPC and M1 are directly involved in planning and execution of skilled locomotion, respectively, such as when overcoming obstacles or perturbations. Moreover, gait deficits present in Parkinson's Disease have driven research into the role of the basal ganglia during locomotion, revealing an influence via modulation of downstream brainstem nuclei. Yet, how these cortical and subcortical areas coordinate their activity to modulate spinal circuits during skilled locomotion is not well defined.

To address this question, we have designed task based on delivering rapid mechanical perturbations to head-fixed mice running on a large spherical treadmill. Our behavioral paradigm applies these perturbations from a total of 12 different positions spanning 6 locations and 2 different elevations. This allows us to elicit a broad range of behavioral responses, which are determined by the actuator's location and the timing of the perturbation relative to the animals' ongoing gait cycle. To study the role of cortico-basal pathways in sensorimotor integration, we are recording from limb-specific subregions of sensorimotor cortices, downstream basal ganglia projections, and relay centers in the motor thalamus projecting back to cortical areas. Simultaneously, we are tracking whole-body 3D kinematics using a deep learning-based pipeline for marker-less pose estimation to have a complete view of how neural dynamics within these regions contribute to sensorimotor corrections during locomotion.

Our analysis is focused on understanding how the cortico-basal ganglia system translates sensory responses into motor corrections. Our first findings show an increase in the dimensionality of cortical and striatal activity during perturbations, as well as the presence of rapid perturbation-specific responses in both areas, with similar latencies. By combining geometric and dynamic characterizations of neural population activity across cortico-subcortical regions and the relation of these changes with inferred sensory feedback and motor responses, we aim to provide a description of how supraspinal centers modulate skilled locomotion.

2-C-38 - Intervention of freezing of gait in a neuromusculoskeletal model

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<u>Details</u>

The ability to initial and terminate locomotion in response to different situations is an essential survival strategy in mammals. This flexibility of locomotion is thought to be mainly regulated by the brainstem and spinal cord. Although freezing of gait (FOG), a pathological phenomenon seen in conditions such as Parkinson's disease, deprives individuals of flexible locomotion and increases the risk of falls, its pathogenesis remains unclear. In this study, we investigated the pathogenesis of FOG and its subtypes using a two-dimensional neuromusculoskeletal model. This model consisted of a body with seven links and 18 muscles, as well as a neural system including the brainstem and spinal cord. We set the anterior flexion angle of the trunk to 6° and the gait velocity to around 0.8 m/sec. These values were based on previous studies that investigated the statistical characteristics of Parkinson's disease. After internal parameter optimization using standard genetic algorithms, the model was able to walk successfully. Under abnormal brainstem activity conditions, we investigated whether FOG could be observed by modifying the parameters of the pedunculopontine nucleus (PPN) and cuneiform nucleus (CnF) models in the brainstem during the walking. Using an FOG-identifying algorithm, we detected FOG events among the generated 40,000 parameter sets. Furthermore, we investigated whether continuous CNF and PPN stimulation, assuming electrical stimulation or sensory cueing, would improve FOG events. Such computational simulations can potentially facilitate the development of individualized therapeutic interventions, which may contribute to improved treatment outcomes.

2-C-39 - The role of fidgety movements in infant locomotor development revealed by longitudinal comparisons of muscle synergies

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<u>Details</u>

Motor development is generally regarded as a gradual process in which infants acquire skills through continuous practice^{1,2}. Some early stages of development serve as critical precursors, influencing and predicting performance in subsequent stages³. Among these, general movements occurring from birth to 5 months are key indicators that can predict neurological disorders later in life^{4,5}. Specifically, fidgety movements (FMs) observed between 2 to 5 months have garnered considerable attention, as their absence is linked to cerebral palsy, with a predictive accuracy of up to 98%^{6,7}. Despite this, our understanding of why FMs are predictive of later behaviors is limited to observational studies⁸ and kinematic examinations^{9,10}, and the underlying neural mechanisms remain unclear. To explore this, we propose that FMs may serve as potential precursors to independent locomotion and aim to investigate the intrinsic connections between these developmental stages.

One prevailing theory explaining the neural basis of diverse behaviors is motor modularity^{11,12}. This theory suggests that a limited set of motor modules are encoded within the spinal cord and are modulated over time by supraspinal regions. Through flexible combinations, these modules facilitate efficient execution of various movements. Motor modules are often quantified using a mathematical

model of muscle synergies (MS)¹³, where each muscle-synergy vector represents a specific synergistic pattern across multiple muscles. MS for a given task are extracted from simultaneous recordings of muscle activities across several channels^{14,15}, allowing us to identify the exact muscle coordination patterns activated and their relative contributions. Hence, by comparing MS across stages of FMs and walking, we can observe the development of neuromotor mechanisms and explore their interrelationships^{16,17}.

In this study, we longitudinally recorded surface electromyography (EMG) signals from 10 muscles in each limb, along with synchronized video recordings, from typically developing infants (n=22) at three key developmental stages: FMs (age of 2.9-4.5 months old), supported walking (SPWalk, 7.1-13 months old), and independent walking (IPWalk, 12.3-17.7 months old). The recorded muscles included tensor fascia latae (TFL), adductor longus (AL), vastus lateralis (VL), vastus medialis (VM), rectus femoris (RF), hamstrings (HAM), tibialis anterior (TA), gastrocnemius medialis (GM), gastrocnemius lateralis (GL), soleus (SOL). The MS at each stage in each infant were extracted from the matrix of multi-channel preprocessed EMG signals using non-negative matrix factorization algorithms^{14,18}. Our longitudinal and cross-sectional analysis of MS revealed that FMs were the most significant predictor of MS during IPWalk, as their contribution of MS preceding other same-stage behaviors such as kicking, co-contraction, and non-fidgety movements. Additionally, MS patterns associated with IPWalk developed from both FMs and SPWalk, since they were either preserved or reconstructed from previous MS through merging or fractionation. This suggests that the MS required for independent locomotion are already present at earlier stages, even as early as infants' 3 months old, providing an electrophysiological explanation for the strong predictive power of FMs.

In conclusion, this study enhances our understanding of the neuromotor mechanisms underlying FMs, SPWalk, and IPWalk by analyzing their associated MS. Moreover, we investigated how the MS of IPWalk evolve from earlier stages, showing that early MS are either preserved or recombined to support the development of mature MS. However, it remains unclear why some MS are entirely retained while others undergo structural modifications through merging and fractionation. Further research is needed to uncover the functional significance of these MS changes throughout infant locomotor development. Notably, this process considers to be gradual and fine-tuned, as IPWalk rarely requires entirely new MS. Besides, these findings hold significant implications for pediatric rehabilitation, particularly in the early identification and correction of abnormal MS patterns to reduce the risk of developmental disorders.

2-C-40 - Assessing trade-offs between risk and effort during walking

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Details

Typically, we choose walking speeds based on an effort-minimization strategy, where effort is often quantified as the energy required to move a given distance. However, when balance is challenged, we may prioritize minimizing the risk of falling over minimizing physical effort, introducing a trade-off. Our current understanding of how people balance effort and risk to guide walking is limited. Thus, we aim to explore how young adults trade off physical effort and the risk of falling during walking.

Participants' self-selected walking speed on the treadmill was obtained using a staircase protocol. Then, treadmill speed was increased by 0.1 m/s to determine participants' fastest comfortable walking speed.

We used both speed values to define six participant-specific walking speeds, ranging from values below self-selected to the fastest comfortable speed. To introduce balance disturbances, we generated unpredictable increases in belt speed equal to 20%, 30%, 40%, and 50% of participants' self-selected speed.

We adapted a decision-making protocol to walking by asking participants to choose between an effortonly and a risky condition. Participants experienced two sequential walking bouts (a trial) consisting of a constant speed, effort-only condition at one of the six speeds without perturbations and a risky condition at their self-selected speed with two perturbations (one per leg). After each trial, participants were asked to choose which bout they would prefer to repeat for five minutes. Each trial was repeated five times, totaling 120 trials across four blocks of 30. To ensure that participants considered the consequences of their choices, we informed them that they would perform one of their chosen bouts at the end of the experiment.

Physical effort was quantified objectively using metabolic rate and cost of transport and subjectively using the rate of perceived exertion. Risk of falling was estimated as perturbation magnitude. These metrics were linearly combined into six different models, to represent the utility of each bout, reflecting the relative weight of risk and effort considered by each participant. A softmax function was then applied to the utilities of each bout to calculate the probability of choosing the risky bout.

Across participants, the model that included both metabolic rate and cost of transport as measures of effort, along with perturbation size as a measure of risk, best explained their decisions. On average, the models had a sensitivity of 0.97 +/- 0.01 and a specificity of 0.57 +/- 0.08. The relative influence of risk varied considerably across participants as the coefficient for risk sensitivity ranged from -0.33 to 6.8, with some participants being less sensitive to risk while others were very risk sensitive. Overall, the results from this study demonstrate that people weigh both risk and effort when making walking-related decisions, but the relative weight of each factor varies in a subject-specific manner.

D – Integrative Control of Movement

2-D-42 - MEG reveals simultaneous intrinsic and extrinsic motor plans in parietofrontal cortex

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Details

It is often assumed that the brain first converts sensory inputs into extrinsic movement plans before computing intrinsic muscle commands tailored to limb posture. However, where, how, and when this transformation occurs in the human cortical arm movement planning network remains largely unknown. Here, we use high spatiotemporal resolution magnetoencephalography (MEG) combined with a pro-/anti-wrist pointing task in two opposing forearm postures to investigate this question.

We computed cortical source activity in 16 previously identified bilateral cortical areas (Alikhanian et al., *Frontiers in Neuroscience*, 2013). Previous studies comparing pro/anti trials revealed a posterior-to-anterior sensorimotor progression from α -/ β -band sensory activity to β -band motor activity, followed by a recurrent anterior-to-posterior motor code progression (Blohm et al., *Cerebral Cortex*, 2019). Further,

we demonstrated how these signals integrate with hand use to form a hand-specific movement plan (Blohm et al., *J Neurophysiol*, 2022).

Here, we contrasted oscillatory activity related to opposing wrist postures to identify posture coding and examine when and where extrinsic and intrinsic motor codes emerge. We found distinct but overlapping networks coding for posture (γ -band) and posture-specific movement plans (α - and β -bands). Some areas, such as pIPS, exhibited only extrinsic motor coding, while others, such as AG, encoded only intrinsic motor signals. However, many regions encoded both extrinsic and intrinsic movement in parallel. In these areas, intrinsic coding generally emerged first, with the earliest intrinsic activity appearing in POJ around 180 ms after target cue presentation.

Our findings suggest a direct feed-forward transformation from sensory to intrinsic motor coordinates for rapid motor control, alongside parallel computations of extrinsic motor coordinates supporting higher-level aspects of visually guided action, such as spatial updating and internal performance monitoring.

2-D-43 - Feedback gains reflect unfolding decisions during ongoing actions

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<u>Details</u>

Many studies have suggested that during deliberation, decision-related processes have a strong influence on the preparatory state of the motor system. In humans, this has been shown by measuring corticospinal excitability and proprioceptive feedback gains, but mainly in experimental paradigms where decisions were made prior to initiating movement ("decide-then-act" scenarios). It remains to be established whether the same conclusions hold in natural situations where decisions can occur during ongoing movement ("decide-while-acting" scenarios). Here, we assessed whether deliberation processes influence the preparatory state during ongoing movements by measuring rapid motor responses to mechanical perturbations of the moving limb. Participants (N=26) performed a dynamic tracking task, in which they decided whether to continue tracking a moving target or switch to a new one. In 33% of trials subjects simply tracked a blue target moving across the workspace ("No Choice" trials). In another 33%, midway through the tracking movement, an alternative blue target appeared orthogonally to the right of the current tracking trajectory, and participants were free to either continue tracking the original target ("Free Continue" trials) or switch to reach to the new one ("Free Switch" trials). Subjects switched targets approximately 40% of the time. The remaining 33% of trials were Forced Choice trials, in half of which the alternative target color instructed participants to switch (green target, "Forced Switch" trials) and in the other half it instructed them to continue tracking (red target, "Forced Continue" trials). In 75% of all trials, a small mechanical load that pushed the hand away from the alternative target was briefly applied to the arm at one of three times (0, 200 or 250ms) after its onset. This allowed us to estimate feedback gains by measuring evoked EMG activity in the lateral triceps, an agonist muscle for movement toward the alternative target. As expected, we found that at 200 and 250ms after target presentation, feedback gains in "Free Switch" trials were significantly higher compared to "Free Continue" or "No Choice" trials, reflecting the preparation to switch. Most interestingly, however, we also found that feedback gains were higher in "Free Continue" than in "No Choice" trials at 200ms, as if the motor system was transiently engaging the muscle while the new target option was being considered, even though it was ultimately rejected. Indeed, this effect promptly disappeared at 250ms, as if at this time the decision had been made to ignore the new target. These

effects were not observed in "Forced Continue" trials, suggesting that it is the deliberation process, rather than an externally instructed goal change, that dynamically influences the motor system. These findings provide further support for the notion that cognitive and motor processes are interdependent, and interact even during "decide-while-acting" scenarios.

2-D-44 - Cerebellar EEG oscillation related to repetitive vocalization in human

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Cerebellar EEG oscillation related to repetitive vocalization in human

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ABSTRACT

The present study investigates EEG oscillations and related neural generators involved in the production of the repeated syllable [pa], with a particular focus on the cerebellum's role in coordinating the consonant [p] and the vowel [a]. It is well established through fMRI research that cerebellar activity overlaps in both speech and song production and perception. Cerebellar lateralization depends on the rhythmic or prosodic nature of vocalization. Studies have shown that singing involves greater activation of the left cerebellar lobule, while speech production predominantly engages the right cerebellar lobule.

Despite its high spatial resolution, fMRI is less precise when investigating the brief time window of syllable articulation, which occurs over a few tens to hundreds of milliseconds. To overcome this limitation, we used EEG to study both cerebellar and cortical involvement in the repetitive production of a simple syllable, focusing on the articulation of the plosive consonant [p] and its transition to the vowel [a]. Specifically, we analyzed the neurological processes involved in consonant articulation preceding the production of [a] and the articulatory preparation for the following [pa] syllable.

We recruited 19 healthy French-speaking students (10 men, 9 women). Each participant completed 20 sequences, each consisting of approximately 100 repetitions of [pa], with their eyes closed. This procedure was approved by the local Ethics Committee. Acoustic and aerodynamic parameters,

respiratory muscle activity, and EEG (64-channel ANT system) were recorded synchronously. All data processing was performed using MATLAB, the EEGlab toolbox, and swLORETA.

To accurately time-lock syllable production events for each [pa], we placed trigger pulses at the onset of intraoral pressure increase, marking the precise moment of bilabial occlusion (syllable onset), and at the onset of intraoral pressure decrease, coinciding with the onset of increased airflow (with a temporal precision of approximately 5 ms). The average syllable duration was 265 ± 30 ms, with the bilabial occlusion phase lasting an average of 106 ± 20 ms. Event-related potential and event-related spectral perturbation analyses (ranging from 0.5 Hz to 200 Hz), as well as inverse modeling, were conducted on the segmented EEG signals of the [pa] syllable, individually adjusted to each participant's average syllable duration and subsequently analyzed in the grand average signal.

We identified EEG generators in the right cerebellar lobule during two distinct periods: the first occurring 10 ms after bilabial occlusion, lasting for 50 ms, and the second appearing 80 ms after lip opening, lasting for 20 ms. No cerebellar activity was detected at the moment of lip opening. We propose that these two short phases of cerebellar activity contribute to the articulation process, coordinating the transition between the end of one syllable and the preparation of the next. This suggests a role for the cerebellum as a braking mechanism, particularly during the vowel [a] phase of the syllable.

2-D-45 - Micro offline gains do not reflect offline learning or consolidation of motor sequence memories

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<u>Details</u>

Micro-online gains (MOG) are increases in performance caused by short breaks during early motor sequence learning. These increases have been interpreted as a sign of offline motor-sequence learning, i.e. the formation or consolidation of a motor memory of the sequence that relies on neural processes during rest. We present a series of behavioral experiments that cast serious doubt on this interpretation. Replicating the finger-sequence paradigm, for which MOGs have been first reported (Bönstrup et al. 2019), we found MOGs for short breaks early in sequence learning as in the original experiment. However, when adding a control condition with random sequences (missing from the original paper), we found equivalent MOGs in the absence of sequence learning. The improvements during the breaks were solely caused by a slowing during the online phases, which then recovered during the break. Sequence-specific learning (as measured by a difference between sequence and random group) was only evident during the online phases of learning. In the sequence group, gains due to sequence-specific learning overlap with the slowing, leading to the lack of behavioral changes within early phases of training, a phenomenon that triggered the original misinterpretation. We then investigated MOGs in the context of a sequential reaching task, which was used by Griffin et al. (2025) in non-human primates. When we repeated the experiment (which in this case included a random control condition), in a group of human subjects, we were unable to replicate the reported results. Instead, we again found clear evidence of sequence-specific learning during the first two online phases of practice (each 10 trials). No clear evidence for offline gains was found, likely caused by the fact that there was no slowing in the random condition. We also extended the experiment to show not just the next, but multiple future targets ahead. This manipulation separates the learning of predicting which target comes next from the motor optimization of a sequence. Even with multiple targets visible, we found sequence-specific learning mainly during the online phases, but not during the break. Overall, our results suggest that the neural events during short breaks between motor sequence learning may not be related to the formation of a motor memory.

<u>2-D-46 - The importance of 3D information in virtual obstacle avoidance: Effects of perceptual uncertainty and feedback</u>

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<u>Details</u>

Here, we investigated if and how obstacle avoidance in virtual environments is influenced by perceptual uncertainty and feedback. Previously, we looked at how manual obstacle avoidance movements for both real and virtual obstacles are affected by perceptual uncertainty (light level manipulations) and assumptions about action consequences (obstacle fragility manipulations). We found that decreasing light levels resulted in increasing safety margins for real and virtual obstacles. However, in many VR applications, we do not perceive the movement of our actual hand but that of a virtual representation that is interacting with virtual objects of varying degrees of complexity (e.g., 2D or 3D representations). Frequently, some form of feedback (visual, auditory, and/or haptic) is used to signal contact with targets or collisions with obstacles. In two experiments, we investigated the effects of perceptual uncertainty (varying contrast) and visual feedback on obstacle avoidance movements when visual information about the moving hand is provided by a sparse virtual representation. We varied the visual complexity of the obstacle between experiments: 2D image in Experiment 1 (N=22), and virtual 3D object in Experiment 2 (N=24). Experiments were conducted in a mirror setup. A monitor projected representations of the target, obstacle, and virtual hand onto a semi-transparent mirror so that they appeared to be in the workspace below the mirror where participants moved their hand. The hand was represented by two white rectangles, following the movement of two motion tracking markers placed on the index finger, and the left side of the hand. Participants did not see their actual hand. The obstacle and the target were white squares lighter than the black background of the workspace (0.3 cd/m²). The obstacle and target squares as well as the two hand markers had either a luminance of 75 cd/m^2 (hight contrast) or 0.4 cd/m² (low contrast). In Experiment 2, a real object was placed above the mirror so that its projection appeared in the workspace centred in the obstacle square. In the feedback conditions, the obstacle and target squares changed colour to a bright red and green, respectively, if the hand markers overlapped with them. In the no-feedback conditions, the appearance of the obstacle and target squares did not change upon contact. Participants' task was to move their hand from a start position past the obstacle to a target location. For each combination of light level and feedback condition, participants performed 20 repetitions under full vision while the movements of their index finger and hand were tracked using an electro-magnetic motion tracker. We found that when the obstacle was a 2D image, the effects of perceptual uncertainty and feedback on safety margins were negligible. However, adding the virtual 3D object resulted in behaviour similar to that observed in real environments highlighting the importance of 3D information for natural movements.

2-D-47 - Pupil size reflects the attenuation of motor fatigability by reward

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<u>Details</u>

Introduction

Reward has been shown to enhance motor performance even in a fatigued state, yet the underlying mechanisms remain unclear. Previous research suggests that reward increases the effort invested into a movement. Fast, repetitive movements induce motor fatigability, here quantified as a decrease in movement speed. This phenomenon is referred to as motor slowing. In monkeys, reward-induced increase in movement effort has been associated with heightened locus coeruleus (LC) activity. However, the LC's role in mitigating motor fatigability through reward remains unexplored. LC activity, which correlates positively with pupil size in humans, can be approximated by measuring pupil size under constant ambient lighting. This study investigates whether the LC might contribute to the mechanisms by which reward reduces motor fatigability. Specifically, we hypothesized that reward-driven changes in pupil size would reflect the reward's impact on motor slowing.

Methods

25 healthy participants (age: 27 ± 4y; 13 females) completed a combined wrist tapping and reward task. Participants tapped at their maximal voluntary speed between two force sensors by flexing and extending their right wrist for 40s per trial. After 20s of tapping, a cue signalled whether the trial was a reward or a neutral trial. In reward trials, participants could win 1 CHF by tapping faster on average than in the previous reward trial. No rewards could be won in neutral trials. The experiment included 10 trials per condition (pseudorandomized). Linear mixed-effects models (LMEM) were used to test the effect of time (0-10s, 10-20s, 20-30s, 30-40s) and condition (neutral vs. reward). Cue-evoked changes (difference between mean 5s post-cue and mean 5s pre-cue) were correlated with cue-evoked changes in tapping frequency. The research question, hypotheses, analytical approach and sample size were pre-registered (https://osf.io/zmpuq).

Results

While motor slowing was successfully induced (LMEM: main effect Time p<.001), confirming that participants entered a fatigued state, the presentation of the reward cue significantly increased tapping frequency (Time x Condition interaction: p<.001). The reward cue triggered pronounced pupil dilations (Time x Condition interaction: p<.001). Additionally, reward-cue evoked changes in pupil size positively correlated with changes in tapping frequency (r=.46, 95%-CI: [.011, .721]), highlighting a link between pupil size and motor performance.

Conclusion

Our findings demonstrate that offering reward can attenuate motor fatigability. The positive correlation between reward-induced changes in pupil size and tapping speed suggests that pupil size, as a proxy for LC activity, may reflect the effort invested in the task. These findings align with research in monkeys showing that reward enhances the effort invested into a movement through increased LC activity. Our results suggest a potential contribution of the LC to the effect of reward in a fatigued state.

2-D-48 - Cognitive maps of sensorimotor programs

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<u>Details</u>

Humans have an exceptional ability to link movements with external cues. For example, playing the violin requires adjusting the force and timing of bow movements with sheet music. However, how the brain relates sensorimotor features with external cues remains unclear. One potential explanation lies in the cognitive map theory, which posits that the brain constructs mental representations of spatial and abstract environments to guide memory and action. Cognitive maps are instantiated in the hippocampus, retrosplenial, and entorhinal cortex, where grid cells in the entorhinal cortex represent environments through receptive fields arranged in a hexagonal pattern.

This study investigated whether cognitive maps support sensorimotor representations and how memory and sensorimotor regions interact to link external cues with motor actions. Twenty-four participants learned to associate isometric hand-grip exertions with external cues varying in force and time, organized in a 2D force-time space. Participants then performed a motor-space navigation task while undergoing functional magnetic resonance imaging. The task consisted of: (1) localization, where participants performed an exertion and matched the exertion's force and time to a hidden cue, and (2) navigation, where participants mentally computed the distance between the localized and target cues in the force-time space.

During navigation, activity in the entorhinal cortex exhibited six-fold periodicity, consistent with a hexagonal grid-like code. This extends the entorhinal cortex's role in encoding bodily states beyond position and velocity to include force and time, which are essential for physical interactions. Dynamic causal modeling revealed that during localization, the retrosplenial cortex integrated inputs from the hippocampus, entorhinal cortex, and sensorimotor regions (e.g., primary motor cortex). During navigation, the retrosplenial cortex projected to the entorhinal cortex, facilitating navigation in the force-time space.

Pattern component modeling showed that the primary motor cortex prioritized force over time when encoding exertions, consistent with participants' subjective ratings, where changes in force levels felt more effortful than changes in time levels in the force-time space. In contrast, the retrosplenial cortex balanced force and time representations, reflecting task demands that required evaluating both dimensions equally. These results suggest that different brain regions can have different representations of force-time space, which are integrated to allow for the flexible navigation of multidimensional sensorimotor environments.

Together, this study demonstrates that cognitive maps encode sensorimotor information. Memory and sensorimotor regions interact to associate precise motor actions with external cues, with the entorhinal cortex representing higher-order bodily states and the retrosplenial cortex acting as a hub for integrating and balancing sensorimotor information.

2-D-49 - Auditory-motor integration dynamics in the posterior tail of the striatum

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Details

We developed a novel manipulandum paradigm in head-restrained mice to test how mice learn auditory cued forelimb movements. We call it the DAAS task, for dynamic auditory action selection. Mice were trained to push or pull the manipulandum depending on the frequency of the auditory stimulus. We

analyzed how the trajectory of forelimb movements became more stereotyped with learning, finding reduced variability in tortuosity and area visited.

We performed two-photon microscopy through a chronically implanted GRIN lens of neurons expressing GCaMP7f in the tail of the striatum. The tail is a region of dorsolateral striatum that receives unique dopamine input compared to other striatal regions and glutamatergic synaptic input from auditory and visual cortical and thalamic regions, as well as motor cortical input. It has remained unclear whether the tail of the striatum is primarily involved in sensorimotor integration, similar to more anterior striatal regions, or rather more "associative" aspects of learned behaviors.

We imaged calcium signals in populations of D1- and D2-expressing spiny projection neurons (SPNs) in the tail of the striatum as mice learned and performed the DAAS task. We observed robust activation patterns in SPNs correlated with both auditory cue and forelimb movement, with some cells showing sustained increases and others a biphasic signal with decreases below baseline. Activity patterns were classified into distinct clusters, which were stable over multiple days of auditory-motor learning. Fascinatingly, individual neurons could switch clusters across days within these stable clusters. Moreover, cellular activity of both D1- and D2-SPNs was more robust on correct (rewarded) trials, independent of the movement performed. Our results thus far support a role for the tail of the striatum in integrative, associative aspects of motor learning.

2-D-50 - Preliminary evaluation of a neurally controlled powered knee-ankle prosthesis

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<u>Details</u>

Lower-limb amputation affects the mobility and quality of life of roughly 600,000 people in the United States [Ziegler-Graham, Arch Phys Med Rehabil, 2008]. Most people with above-knee amputations use passive prostheses, which can provide resistance at the knee and ankle joints but do not provide the user with power. This lack of power can lead to slower walking, gait asymmetry, and difficulty navigating stairs and slopes [Goldfarb, JPO, 2013]. Despite advancements in and commercialization of powered prostheses (e.g., Össur Power Knee), widespread clinical success remains limited, in part because users do not have volitional control of their devices. Efforts to employ neural control with surface electrodes have been hindered by signal drift, impulse artifacts, and cross-talk, which preclude reliable translation [Yeon, EMBC, 2021]. The combination of two surgical innovations—the Agonist-Antagonist Myoneural Interface (AMI) and implanted electrodes via osseointegrated implants (eOPRA)—may overcome these limitations. A recent study leveraging AMI and eOPRA to enable agile control of a powered knee prosthesis allowed users to navigate dynamic terrain, but walking symmetry and speed were still hindered, likely due to insufficient ankle power [Shu, submitted, 2024].

Here, we present a powered knee-ankle prosthesis, which is an upgraded version of hardware previously published. Key upgrades to the system include new joint encoders and a 6-degree-of-freedom load cell to improve reliability, software changes to increase bandwidth, and an optimized electronics mount to mitigate thermal issues caused by motor drivers. Additionally, we developed a custom power board to supply energy efficiently to multiple motor drivers, the onboard computer, and other peripherals, ensuring robust and reliable performance.

When we tested our upgraded prosthetic on a subject with the AMI and eOPRA surgical constructs, they were able to successfully ambulate with the powered knee-ankle system. Not only did the subject

display increased preferred walking speed and symmetry, but they also showed marked improvement in volitional free-space control. In a pilot free-space experiment, the subject was seated and physically separated from the prosthesis. They were tasked with aligning the prosthesis's toe, midsoul, and heel with a target. Each of these three conditions was repeated 24 times. The experiment was then repeated with the subject blinded to visual feedback (Supplemental Figure 1). Although the blinded results showed reduced extension across the board, the subject demonstrated a significant ability to replicate movements without feedback.

This work introduces a powered knee-ankle prosthesis that addresses key limitations of previous designs. The user demonstrated improved gait and consistent control of the leg. Enabling volitional control of a prosthesis is critical for providing people with amputations improved agile control and gait symmetry.

<u>2-D-51 - Prediction of sensory attributes of action-outcome shape action kinetics early during</u> <u>movement</u>

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Details

The kinetics of goal-directed actions are shaped by multiple factors including the desired goal (e.g. to catch a ball), and various constraints (e.g. using my non-dominant hand because my dominant is currently occupied). One factor that has been shown to influence action kinetics is the association of the action with a sensory outcome. For example, action kinetics during a button-press have been shown to be sensitive to the absence or presence of a causally related auditory outcome, and comparison of force profiles shows that participants apply less force when an auditory outcome is (vs. is not) expected.

In the current study, we further set to characterize how expected attributes of stimulus outcome (intensity) shape the kinetics of the triggering action (applied force), even when the two are unrelated. Specifically, (1) whether the amplitude of expected stimulus outcome modulates action kinetics; (2) whether such modulations are related to foreknowledge (prediction) of the outcome stimulus amplitude; and (3) whether such force modulations permeate to kinetics of early actions embedded in an action sequence.

Participants (N = 24) pressed buttons that triggered an auditory sound of either high or low amplitude across experimental conditions while the force profile of button presses was measured. Results show an inverse relationship such that when outcome amplitude is known in advance, participants applied more force when the expected intensity of the outcome was low (vs. high intensity outcome). However, when sound amplitude could not be predicted in advance (i.e. by randomizing the association between buttons and sound intensity), no modulation of applied force was found. In another group of participants (N = 24) we replicated the force modulation effect in the predictable condition and further show that flipping the causal order between action and sound abolishes force differences related to sound amplitude. In other words, when participants press buttons in response to high/low amplitude sounds (instead of generating sounds by button presses), participants applied similar force levels. The results of these studies show that predicted attributes of stimulus outcome are embedded in action kinetics.

Finally, we examined whether such predictions also affect the kinetics of early actions within an action sequence. To this end, participants (N = 40) performed single or double taps which generated (or not) a
sound immediately following the last tap in the sequence. Single tap results replicate previous findings, showing that participants apply less force when the button press is associated with expected sound outcome. Interestingly, this force modulation was also seen in the force profile of the first tap in the double-tap sequence. In other words, the applied force in the first (silent) tap was lower when the second tap in the sequence was associated with a sound compared to when the second tap did not generate a sound. Thus even though the first tap is temporally and causally separate from the actual sound event, it is still affected by prediction of future outcome. Taken together, our results demonstrate that prediction of future action-outcome attributes shapes action kinetics in early stages of movement.

2-D-52 - Brain mechanical properties relate to decision-making and movement behaviour

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<u>Details</u>

Prior work has shown an integrated network between decision and motor circuits with nonhuman primates. Aligned with an integrated decision and motor network, our recent behavioural work showed that reaching movements reflect the ongoing deliberation process—prior to a decision. Neuroimaging studies with humans have used magnetic resonance elastography (MRE) to characterize microstructural integrity, by quantifying brain mechanical properties (i.e., stiffness and damping). Brain stiffness and damping relate to cognitive functions, such as adaptive-thinking and memory. Yet past work has not linked microstructural integrity to joint decision and motor behaviour. Here we tested the idea that brain microstructural integrity relates to deliberation and its corresponding expression via movement.

We used our recently developed task that allows us to probe the influence of deliberation on movement, prior to a decision. Participants grasped the handle of a robotic manipulandum with their dominant hand. They began each trial with their hand in a start position. Forward from the start position, they observed 15 tokens between two potential targets. Once they left the start position, the tokens individually moved into either the left or right target. Participants were instructed to select the target they believed would end up with the most tokens, prior to all 15 tokens entering the targets. Participants indicated their decision by simultaneously pushing a button with their non-dominant hand and moving their cursor into the selected target. Interleaved with pseudo-random token patterns were biased token patterns, where the first three tokens moved into the left target (left bias) or right target (right bias). These token patterns allowed us to manipulate the deliberation process. We recorded decision time and accuracy. We also recorded lateral hand position, prior to a decision, to test whether deliberation influenced movement. We found the same decision times for left and right bias token patterns differentially impacted the lateral hand position prior to a decision (p = 0.002).

All participants underwent an MRE scan to quantify brain area stiffness and damping. We focused on brain areas within the basal ganglia, intraparietal regions, and frontal cortex, since in non-human primates these regions show neural activity during deliberation. We found that both inferior parietal cortex stiffness and putamen stiffness lateral were positively correlated with lateral hand position (p = 0.041 and p = 0.006, respectively). We also found that caudal anterior cingulate damping was positively correlated with decision time (p = 0.005) and decision accuracy (p = 0.016). Collectively,

our findings suggest that the microstructural integrity of brain regions involved with the integrated decision and motor network may contribute to deliberation and its influences on movement.

<u>2-D-53 - Dynamic connectivity between the primary and premotor cortices during Ipsilateral and</u> <u>Contralateral reaching-to-grasp movements in Macaque Monkeys</u>

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Details

Movement-related neural activity is distributed across multiple cortical areas. Hand movements, such as grasping an object, require the coordinated activity of neuronal populations in several areas, including the primary motor cortex (M1) and the dorsal (PMd) and ventral (PMv) premotor cortices. Differences in the neural network properties of these areas, which support distinct motor functions, may contribute to functional interactions between them. However, our understanding of intra-hemispheric connectivity between M1, PMv, and PMd remains limited. A better understanding of neural dynamics in information coding and processing is needed. This study hypothesizes that motor area connectivity adapts to support movement during a task. We simultaneously recorded neural activity in the hand representations of M1, PMd and PMv of three male rhesus macaques as they performed a precision grip task with either the contralateral or ipsilateral hand. Connectivity was analyzed using a time-resolved cross-correlation approach between well-isolated neurons, examining temporal alignment with behavioral markers and lag-dependent connectivity within cortical networks during the precision grip task. Significant correlations were quantified using Z-scores. We then compared connectivity patterns between M1-PMv, M1-PMd, and PMv-PMd by measuring coupling strength as a function of task performance, which was defined by the incidence and magnitude of Z-scores. Coupling strength was analyzed separately for each monkey, followed by pooling the results across three monkeys for grouplevel analysis. Marked changes in connectivity pattern were observed across different task phases. At the population level for M1-PMv and M1-PMd, coupling strength was highest during reaching when data were aligned was relative to the go-cue event as well as at the end of grasp when the alignment was with the start of grasp for both arms. However, it was consistently stronger and more defined for the contralateral arm. For PMv-PMd, coupling strength followed a similar trend but was generally lower than M1-related connections, with stronger interactions for the contralateral arm and weaker for the ipsilateral arm. Overall, while peak coupling strength occurred at key movement phases for both arms, intra-hemispheric connectivity was stronger and more structured for the contralateral arm, highlighting its dominant role in motor control. By analyzing the temporal dynamics of lag, as an indicator of directionality, in M1-premotor connectivity, we observe that premotor areas initially lead M1 in high coupling periods. This suggests a dynamic shift in influence, where premotor areas drive M1 activity before the directionality of interaction reverses. This study enhances human research by using high-resolution invasive recordings to examine motor network interactions. Understanding these dynamics can help identify neurological disruptions and guide new therapeutic approaches.

<u>2-D-54 - A shared-control AI-iBCI system for seamless navigation in real-world scenarios using virtual</u> reality in Macaque monkeys

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<u>Details</u>

Intracortical brain-computer interfaces (iBCIs) have demonstrated significant potential for enabling users to control complex systems in laboratory settings. However, these systems have not yet been implemented on a large scale in home environments, leaving a substantial gap in their ability to help paralyzed patients regain independence and improve quality of life. Furthermore, current iBCIs are often physically and mentally demanding for users, making extended daily use impractical.

To address these challenges, we developed a **blended AI-iBCI system** for seamless navigation in virtual reality (VR). This system combines artificial intelligence (AI) with neural decoding to enable **continuous shared control**. The proposed approach effectively manages complex scenarios, such as avoiding sudden obstacles, which are particularly challenging for pure BCI systems. The BCI component decodes movement intentions from intracortically recorded activity in primary motor and dorsal and ventral premotor cortex and converts it into velocity commands for navigating virtual environments. Meanwhile, the AI component interprets these intentions within the context of the environment, compensating for the noise in the neural decoding and continuously assisting users in reaching their goal. Compared to pure BCI systems, the blended AI-iBCI approach enhances performance, reduces the need for extensive training, and lowers cognitive load during tasks.

We validated our system using online BCI data from two macaque monkeys performing VR navigation tasks. In the **first task**, involving obstacle avoidance with fixed obstacles, success rates improved from 49% with full BCI control to 81% with shared AI-BCI control across 12 sessions. In the **second task**, designed to assess the adaptability to changes in intention, obstacles dynamically appeared on the path to the target. Success rates increased from 44% under full BCI control to 71% with shared control—an improvement of 38% (N = 9 sessions). Multielectrode neural recordings from the motor and premotor cortex were used to train the decoder, enabling precise decoding of movement intentions. The shared control mechanism with the AI facilitated smoother trajectories, achieved higher success rates during obstacle avoidance, and improved adaptability to environmental challenges, such as dynamic target repositioning, compared to traditional BCI systems.

We also investigated the interplay between AI and BCI components, focusing on their mutual adaptation and the benefits of shared control. Preliminary results indicate that the system supports learning and neural plasticity, enabling users to achieve near-natural control even in complex and unpredictable scenarios.

This work bridges computational motor control, shared autonomy, and adaptive system design, emphasizing the transformative potential of blended AI-BCI systems to revolutionize navigation and interaction in both virtual and real-world settings.

<u>2-D-55 - Evidence of nonmotor prediction errors in the human cerebellum during reinforcement</u> <u>learning</u>

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<u>Details</u>

The cerebellum has long been considered a crucial hub for sensorimotor learning. In this domain, the cerebellum is thought to act as an internal forward model, making predictions about the outcomes of motor commands and computing prediction errors based on discrepancies between predicted and actual outcomes. The prediction errors calculated in the cerebellum are then used as teaching signals

to refine actions and reduce error. Numerous studies highlight how the circuitry of the cerebellum is optimized for prediction error-driven sensorimotor learning. More recently, there has been growing interest in the role that the cerebellum might play in nonmotor, more cognitive forms of learning, particularly in situations that also involve prediction and prediction error. For example, recent work in both rodents and nonhuman primates provides strong evidence that the cerebellum is indeed involved in core neural computations associated with reinforcement learning (RL; Wagner et al., 2017; Heffley and Hull, 2019; Hull, 2020; Sendhilnathan, Ipata, and Goldberg, 2020). Might the human cerebellum also play a role in prediction-based learning in nonmotor domains as it does in motor learning? In this project, we investigate the role of the cerebellum during RL in humans using fMRI. During the task, participants (N = 21) chose between stimuli that were associated with different reward probabilities and were instructed to use reward feedback to optimize their choices. Crucially, reward contingencies were linked to stimuli, rather than specific actions. Using model-based fMRI analyses, we find evidence that reward prediction errors (RPEs) are represented in the human cerebellum during RL, primarily in bilateral Crus I and II. Further, we find preliminary evidence that the cerebellum is preferentially involved in representing RPEs when latencies between stimuli and reward feedback are short (800ms) versus long (3s), echoing similar results in the domain of sensorimotor learning. Taken together, these results suggest that the cerebellum might perform more generalized error-based learning in both motor and nonmotor domains. In ongoing work, we are investigating whether the cerebellum might play a role in unsupervised, nonmotor forms of statistical learning, which also involves predictive processes.

2-D-56 - Somatosensory inputs to primate primary motor cortex: dual roles in voluntary movement

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<u>Details</u>

The primary motor cortex (M1) receives short-latency somatosensory inputs from the periphery, yet their functional role remains unclear. While it is established that somatosensory-evoked potentials (SEPs) in M1 are dynamically modulated during voluntary movement, the specific role of these inputs and their task-dependent modulation remain poorly understood. To address this, we examined the size and modulation of somatosensory inputs originating from agonist and antagonist muscles during wrist movements in monkeys.

We trained two rhesus monkeys to perform a wrist flexion and extension task using visual feedback. During task performance, we inserted a high-density multichannel electrode (Plexon's S-probe; 32 or 64 channels) into M1 through an implanted cranial chamber to record local field potentials. SEPs were elicited by electrical stimulation of the superficial radial nerve (SR) and deep radial nerve (DR), targeting cutaneous and muscle afferents, respectively, on the wrist extensor side.

We recorded 167 SR-SEPs from 26 sites and 73 DR-SEPs from 11 sites in the M1 of two monkeys. We compared the size of averaged SEPs evoked during the rest and movement periods of flexion and extension trials, analyzed individually. As expected, we observed an attenuation of both SR-and DR-SEPs during movement compared to the rest period.

However, further analysis revealed two unexpected findings. *First*, the SR-SEPs size and the degree of attenuation varied significantly with the depth of the recording site within M1. Specifically, deeper recording sites exhibited smaller SEPs sizes (r=-0.56, p<0.0001) and greater movement-related attenuation (r=-0.31, p<0.05). This enhanced attenuation in deeper M1 regions may serve to reduce

excessive transcortical reflexes triggered by natural reafference, which could otherwise interfere with ongoing movement. Namely, it could help to dissociate the link between self-induced reafference and the M1's direct output to motoneurons (corticomotoneuronal tract) to effectively suppress the excitation of long-loop reflex during movement.

Second, the attenuation of SR-SEPs was significantly smaller during agonistic movements (i.e., flexion) compared to antagonistic movements (i.e., extension) (p<0.0001). This smaller suppression of somatosensory input from the antagonistic side suggests that afferent activity, evoked by the movement-related stretch of skin, may be critical for MI in online body state estimation and the updating of motor commands.

In conclusion, our findings suggest that sensory gating in M1 plays a dual role: suppressing undesired transcortical reflexes and selectively extracting valuable sensory signals essential for motor planning and execution.

E – Disorders of Motor Control

<u>2-E-57 - Galvanic vestibular stimulation reveals disruption of ipsilesional brainstem pathways in</u> <u>hemiparetic stroke survivors</u>

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<u>Details</u>

Background: The spatiotemporal structure of muscle coordination emerges from the interaction of descending cortical, spinal, vestibular, and brainstem pathways (Bartsch and Valero-Cuevas, 2025). Thus, disruptions in brainstem drive following stroke is thought to contribute to pathological synergies (Krakauer, 2005; Li et al., 2019).

Purpose: While the imbalance of cortico- and reticulo-spinal tracts is thought to contribute to pathological synergies, this study aims to exclude the contribution from vestibular motor output —as measured by IMC— following stroke.

Methods: As in Bartsch and Valero-Cuevas (2025), we used galvanic vestibular stimulation (GVS) to investigate the extent to which vestibular input to the brainstem may be disrupted in stroke survivors (n=14) with right hemiparesis, as compared with age-matched controls (n=14). We tested both arms under three tasks: rest, voluntary reaching movement with neutral and abducted shoulder positions while participants were subjected to three stimulus types: Sham, GVS, and No stimulation. sEMG was recorded from: Biceps (Bic) and Triceps Brachii (Tri), Anterior (ADelt), Middle (MDelt) and Posterior (PDelt) Heads of Deltoid, and Upper Trapezius (UTrap); and one neck muscle, Sternocleidomastoid (SCM), as a control for GVS. Pairwise magnitude-squared coherence from EMG was computed in the 8-50Hz frequency range.

Results: We find that the effect of GVS to neck and arm muscles in the paretic side is similar to that in neurotypical individuals, both at rest and during voluntary reaching movements. However, and to our surprise, GVS is greatly suppressed in neck muscles on the non-paretic side —suggesting strong disruptions in ipsilesional brainstem pathways following stroke. Importantly, since stroke-related neural damage occurs at the upper motor neuron level, GVS is likely acting through a presynaptic mechanism on upper rather than intact lower motor neurons. While these disruptions may not affect arm movement, they may have important consequences to balance control in stroke.

<u>2-E-58 - Deep learning-driven EEG analysis for personalized deep brain stimulation programming in</u> <u>Parkinson's disease</u>

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<u>Details</u>

Deep Brain Stimulation (DBS) is an invasive procedure used to alleviate motor symptoms in Parkinson's Disease (PD) patients once medication starts to lose effectiveness. Despite its benefits, the impact of DBS on brain activity and the best way to optimise stimulation parameters remains unclear. Reliable biomarkers that would allow optimising the DBS parameters are needed.

While most work in the search for biomarkers starts from clinical observations of potential neural markers, here we took a data-driven approach and developed an explainable AI method to identify spectral changes in brain activity which relate to the DBS settings. We recorded in-clinic EEG data from 4 PD patients during DBS programming sessions at rest and arm movement. A siamese adaptation of the EEGNet deep learning architecture was trained to determine whether pairs of 1-sec-long EEG segments were recorded under the same or different DBS parameters. We trained a model separately for each patient and DBS parameter, which included changes in electrode contact and stimulation amplitude. Frequency ablation was then applied as an explainability method, to extract the frequency bands learned by the models.

Our models achieved an average accuracy of 78.24% in classifying whether pairs of EEG segments corresponded to the same or different DBS parameters across 7 hemispheres. Ablation studies identified narrow-band gamma oscillations (NBG: 60-90Hz) as the key feature for classifying these changes consistently across all patients and DBS parameters, causing an average accuracy drop of 18.47% when being removed. We found that one of our patients displayed a 1:2 entrainment of brain activity to the stimulation subharmonic, which was learned by our models and made them achieve the maximum accuracy across patients (86.61%). This is in agreement with a few recent studies of the 1:2 entrainment, yet our results highlight the importance of cortical NBG even in the absence of entrainment.

We show a proof of concept demonstrating that the neural response to changes in contact and changes as small as 0.3mA in amplitude can be detected at the cortical level using shallow convolutional networks applied to EEG recordings. The use of data collected during regular DBS programming clinics emphasises the translational potential of our findings. Our findings consistently suggest that cortical NBG (60-90Hz) contain DBS programming-specific information, and features in these oscillations could be leveraged to guide DBS programming sessions and adaptive DBS systems, potentially improving future treatment outcomes for PD patients.

<u>2-E-59 - Comparison of pallidal neuronal responses to voluntary movement between Parkinson's</u> <u>disease and cervical dystonia patients</u>

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<u>Details</u>

The study of brain neural responses to voluntary movement leads to understanding the motor control mechanisms and can contribute to the development of adaptive stimulation methods for Parkinson's disease (PD). Ethical considerations do not allow invasive study of neural responses of the subcortical nuclei in a healthy person. We hypothesize that the neural responses of patients with cervical dystonia (CD may serve as a conditional baseline in studying the hand movements of parkinsonian patients.

We performed intraoperative microelectrode recordings of pallidal single unit activity in four patients with Parkinson's disease and seven patients with cervical dystonia during neurosurgical procedures for deep brain stimulation. All surgeries were performed under local anesthesia. Voluntary motor tests, which involved clenching the hand into a fist upon the researcher's command, were administered intraoperatively to the patients.

We analyzed parameters of pallidal single unit responses to voluntary movements in the two studied groups:, firing rate off neural activity at rest and during motor tests, response latency and duration. We found pallidal cells, responsive by phasic and tonic activity leading or lagging voluntary movement onset in both groups of patients.

Leading responses were comparable in timing between the groups (ranging from -0.2 to -1.3 s). However, lag responses were more pronounced in the PD group: 0 to 0.8 s in PD versus 0 to 0.35 s in CD. The PD group also showed a higher baseline neural firing rate (75 imp/sec in PD versus 42 imp/sec in CD), while the response amplitude was significantly higher in the CD group (39 imp/sec in PD versus 101 imp/sec in CD).

Thus, our results confirm significant differences in neural responses between patients with Parkinson's disease and cervical dystonia. Increased baseline activity and reduced response amplitude in PD patients may reflect motor control dysfunction characteristic of the disease. At the same time, data from CD patients, whose limb movements are unaffected, may serve as a reference for assessing the conditional baseline of neural responses. We suppose that futher research of neuronal responses to different voluntary movements facilitates a more fine-tuned DBS stimulation in PD.

The study was funded by the Russian Science Foundation (23-15-00487).

2-E-60 - A neural interface for EMG-based cursor control after spinal cord injury

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Details

Spinal cord injury (SCI) disrupts communication between the brain and muscles, resulting in severe motor impairment and reduced quality of life. Despite the interrupted communication, residual muscle activity can often be detected from individuals with SCI despite the absence of overt movement; leveraging this residual muscle activity offers a promising opportunity for neural interfacing and functional restoration. Recent studies have shown that discrete finger gestures can be classified from residual muscle activity in individuals with SCI. However, dexterous control of an assistive device requires continuous control signals. Thus, we investigated whether residual muscle activity could serve as a control source for virtual device operation in tetraplegic individuals.

We used blind source separation of high-density surface electromyography signals to extract the spiking of individual motor units in two people with cervical SCI (MRC grade 0/1, no functional hand use).

Participants underwent a screening session to select an attempted finger or wrist action that showed minimal overt movement but evoked clear residual EMG. From this selected action, the activity of 1) a single motor unit, of 2) several motor units pooled together (cumulative spike train [CST]), and 3) the global EMG were used to control the position of a cursor in 1D. Participants were asked to track three target profiles: 1) trapezoidal (ramp and hold), 2) sinusoidal (ramp and vary), and 3) pseudo-sinusoidal (varying frequencies and amplitudes of sinusoids) to assess static and dynamic components of control. Each session was performed multiple times across several weeks to assess learning. One participant also performed 2D cursor control where the discharge rate of two independent motor units was used to control the cursor's x- and y-axis position.

Participants were able to use their residual muscle activity to accurately track all three target profiles. However, single motor unit and their pooled activity (CST) demonstrated superior control performance compared to the global EMG. Interestingly, we consistently identified several motor units in each individual that fired tonically during both attempted movement and at rest, which may explain the relatively poor performance of the residual EMG as a control signal (these units were removed from the CST).

Cursor control accuracy improved over time despite no change in the number of identified motor units, suggesting that functional gains arise from improved control of these neural signals rather than due to increased motor unit recruitment. Preliminary data also shows the feasibility of 2D cursor using the discharge rate of two independent motor units, which is vital for screen navigation.

Our findings underscore the potential of motor unit activity-driven interfaces for enhancing functional independence in SCI. Future work aims to expand control dimensions and refine interface algorithms for broader clinical applicability.

2-E-61 - Impaired rule -based visuomotor integration in Parkinson's disease

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Details

Parkinson's disease (PD) is widely recognized for its motor impairments, but the impact of PD on visuomotor integration—particularly in translating cognitive rules into movement plans—remains insufficiently understood. In this study, we investigated how participants with PD performed in a mirrorreversed motor task (Tippett & Sergio, 2006), which required them to move a mouse in the opposite direction of a visual cursor to reach a target. Nine individuals with PD, 13 age-matched older controls, and 15 younger controls completed this task. Participants also performed cognitive flexibility, sustained attention, and spatial working memory tasks to assess their cognitive functions. We found that PD participants made more directional errors and took longer to reach the target compared to older controls, who, in turn, performed worse than younger adults. However, in a baseline condition without the reversal, PD participants did not differ from older controls. Importantly, their cognitive flexibility (rule-following ability), sustained attention, and working memory performance were also comparable to those of healthy individuals. These findings suggest that impaired rule-based visuomotor integration in PD is not due to generalized cognitive deficits but rather reflects specific challenges in complex visuomotor planning. This emphasizes the need for further exploration of basal ganglia dysfunction in adapting to altered sensorimotor mappings, which could inform interventions targeting the neural control of movement in PD.

<u>2-E-62 - Antiparkinson medication reduces the probability of the multiple step saccade pattern during</u> <u>a memory-guided saccade task</u>

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<u>Details</u>

While it has been well established that people with Parkinson's disease have impaired internally-driven movements, such as memory-guided saccades, the effects of antiparkinson medication on memory-guided saccades are still unclear. Previous studies have consistently found that people with PD have a higher incidence of multiple step saccades than healthy controls during the memory-guided saccade task. This multiple step saccade pattern is an uncommon series of smaller amplitude or hypometric saccades to reach the remembered target location. This is in contrast to typical task performance, which involves making a larger amplitude primary saccade to the remembered location with the occasional small amplitude corrective saccade if needed. It has been proposed to use this saccade pattern as a potential biomarker for PD, yet it is unknown how it responds to antiparkinson medication.

Thirty-three people with PD and 14 older adult healthy controls completed a memory-guided saccade task. Participants maintained fixation on a central point when a peripheral target briefly appeared for 50 ms. Participants were instructed to memorize the target location using peripheral vision. Following a variable delay (0.5 or 5 seconds), the disappearance of the central fixation point served as a cue to make a saccade to the remembered target location. People with PD performed this task over 2 days: 1 after overnight withdrawal from medication (off-meds) and 1 while on their usual medication (on-meds). The order of these conditions was randomized. Healthy controls performed the task once. Multiple step pattern was defined as the occurrence of 3 or more saccades in the direction of the target. This was a binary outcome for each trial. We used generalized mixed model logistic regression to calculate the probability of the multiple step pattern.

Our findings confirm that people with PD have an increased probability of the multiple step pattern to the remembered target compared to healthy controls. In addition, we found that antiparkinson medication significantly reduced the probability of the multiple step pattern compared to off medication. Further analyses will be performed to test our hypothesis that this probability reduction is accompanied by an increase in primary saccade amplitude, which would suggest a beneficial modulation of saccade amplitude by dopaminergic circuits.

<u>2-E-63 - Stable control through sEMG input: evaluating gesture recognition on a population with hand</u> <u>tremor</u>

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<u>Details</u>

Surface electromyography (sEMG) unlocks the potential of neuromotor signals by offering non-invasive decoding of subtle gestures that would otherwise be difficult to discern from camera- or inertial-based

systems. Recent work by our group has demonstrated that generic sEMG decoding models based on neural networks are performant across many people without the need for per-person calibration. In this study conducted under IRB approval, we further investigate the generalizability of our gesture and writing decoding models to a population of patients with varying severity of hand tremor and compare it to that of touch-screen control and typing on a smartphone. Neuromotor tremor conditions affect a sizable portion of the global population, with Essential Tremor impacting approximately 5% of people worldwide and Parkinson's disease affecting over 10 million individuals globally. By studying how our models perform on this cohort, we hope to evaluate how well sEMG can serve as a stable control method for people with tremors and related conditions. We find that decoding accuracy for gesturebased controls on the tremor cohort is similar to that of a non-tremor baseline and, furthermore, pergesture execution times for menu navigation are significantly shorter for sEMG-based controls than the equivalent touch-screen action. Writing proved to be a more challenging task for the model tested; however, we find that domain adaptation techniques can recover performance for the tremor cohort to a level comparable to that of a non-tremor baseline. Together, these results suggest that sEMG can serve as a viable interaction modality across a range of neuromotor capabilities, including for those with tremor conditions.

2-E-64 - Burst propagation in Pediatric Dystonia

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<u>Details</u>

Repetitive bursting and uncontrolled oscillations are features of pathological brain states that have been observed in epilepsy, brain injury, Parkinson's disease, and some forms of dystonia. We use recordings in basal ganglia and thalamus of children undergoing deep brain stimulation (DBS) to validate **a new computational model of dystonia** in which **hyper-synchronous input** to a population of neurons leads to **(1) bursting and uncontrolled oscillations**, and **(2) propagation** of abnormal activity to downstream regions in basal ganglia and thalamus.

Our model differs from prior models in the origin of bursting and oscillatory activity: we show that **hyper-synchronous firing of a small subpopulation of cells is sufficient to destabilize an otherwise stable network**. Prior models of burst propagation have been applied to **epilepsy**; we suggest the same mechanism may underly spread of abnormal activity in both primary and secondary **dystonia**.

Results demonstrate precisely synchronized (within 0.5msec) spike firing between pairs of neurons in the Globus Pallidus internus (GPi) that can be several millimeters apart. Our computational model predicts that hyper-synchronization in an interconnected network causes large-scale bursting and oscillations, and we see bursting and oscillations in GPi. The model further predicts that this will lead to a **propagating chain reaction of bursting and pathological oscillations** that affects otherwise healthy downstream regions in subthalamic nucleus and thalamus, and we see bursting and oscillations in these regions.

We simulate populations of interacting neurons each with membrane dynamics that approximate the Hodgkin-Huxley equations, and we validate the burst propagation model by comparison with single-unit and local field potential recordings in humans.

Deep brain recordings in 15 children and young adults with dystonia are consistent with model predictions of excessive synchronous activity, bursting, and oscillations in regions that are known to be targets for DBS as well as in downstream regions. Therefore we conjecture that excessive synchronous activity is (1) a biomarker of injury, and (2) a cause of abnormal propagating network activity.

2-E-65 - Anticipatory postural adjustments for voluntary arm movements in children with ASD

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Details

While difficulties in voluntary movements, such as catching a ball, are frequently reported in individuals diagnosed with Autism Spectrum Disorder (ASD), they are not included in the official definition of the DSM-5. Coordinated movements rely on a forward model, where predictions of sensory outcomes of an action are updated based on sensory inputs. Such integration is critical to compensate for perturbations even when they result from one's own actions. According to a recent hypothesis, *atypicalities in predictive abilities* may underpin not only motor control, but several aspects of the complex autism phenotype. This study focused on anticipatory postural adjustments (APAs) necessary for maintaining postural balance when raising both arms, comparing autistic and non-autistic (allistic) children.

In allistic adults, control of upright posture requires anticipatory postural adjustments (APAs) before significant upper-limb action to maintain postural stability. Voluntary arm movements generate shifts in the center of mass, and body weight must be shifted prior to such movements to preempt loss of balance. If there are predictive impairments in autistic children, APAs should be reduced or absent in autistic individuals.

15 allistic and 14 autistic children (minimum Non-Verbal IQ: 86) aged 9-12 years were recorded during an arm raising task, where kinematics, ground reaction forces, and EMG of major muscle groups were recorded. Subjects performed repeated arm raises in the sagittal plane from their arms hanging loosely by their side to a vertical position above their head. This task leads to adjustments in 1) the center of pressure within one's base of support and 2) the temporal activation of several trunk muscles required to preempt and compensate for postural instability.

A triple-inverted-pendulum model, with shoulder, hip, and ankle joints and a triangular foot, was used to assess the impact of self-generated arm raises on postural stability. Measured joint angle trajectories starting at movement onset were fed into the model to obtain the corresponding center of pressure (CoP) profile without incorporating predictive adjustments prior to onset. The center of pressure profile from this simulation extended beyond the base of support, indicating postural instability in the absence of APAs.

Experimental recordings of trunk, arm, and lower leg muscles revealed that in allistic children, both the latissimus dorsi and erector spinae showed significant activity prior to movement onset, clearly

demonstrating APAs. In contrast, the autistic cohort did not display consistent anticipatory muscle activity. This difference in muscle activation patterns was seen across trials and subjects and was not explained by differences in movement speed between groups. Our findings provide evidence for altered predictive motor control in autism, supporting the broader hypothesis of atypicalities in predictive abilities in autistic individuals.

<u>2-E-66 - Combining myoelectric interface conditioning with sleep-based targeted memory reactivation</u> to improve motor learning and function in chronic stroke

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<u>Details</u>

An important cause of arm impairment after stroke is abnormal muscle co-activation. Our previous research shows that home-based rehabilitation using a wearable myoelectric interface for neurorehabilitation (MINT) can effectively reduce this abnormal co-activation and improve both arm function and reaching movement in chronic stroke survivors. MINT conditioning maps surface EMG from the co-activating muscles to orthogonal components of cursor movement in customized video games. By placing targets only along the orthogonal axes, this paradigm conditions users to decouple these muscles to succeed in the games.

Here, we investigated a novel approach aimed at enhancing the therapeutic potential of MINT by integrating it with Targeted Memory Reactivation (TMR), a sleep-based technique designed to enhance motor learning. TMR uses auditory cues tied to specific motor actions (such as movements in MINT games) during slow-wave sleep (SWS) to replay, and thus strengthen, the associated motor memories. We randomized stroke survivors with moderate-to-severe arm impairment to two groups. Both groups trained with MINT for 90-min/day, 6 days/wk over 6 weeks; one heard MINT-related sounds (MINT+TMR) and the other heard unrelated sounds (MINT+sham). Each muscle target was paired with a unique sound, and the muscle pairs trained changed every two weeks. For the MINT+TMR group, these muscle-related sounds were played quietly during SWS, as detected by a machine-learning algorithm using heart rate and accelerometry data from a Fitbit. The MINT+sham group heard unrelated sounds during SWS. Performance scores, including time-to-target and co-activation levels between trained muscle pairs, were computed daily, and the timed Wolf Motor Function Test (WMFT) was the primary functional outcome.

To date, 28 chronic stroke survivors have completed the training protocol, with mixed adherence to TMR protocol. MINT+TMR and MINT+sham participants received auditory cues for the first time 2.5 \pm 2.7 d and 4.3 \pm 7.4 d (mean \pm SD; respectively) after their initial MINT session. The two groups heard similar numbers of sound cues each night (122 \pm 59 vs. 119 \pm 62). Interim results showed that the MINT+TMR group exhibited significantly faster improvement in weighted time-to-target performance than the MINT+sham group (p=0.007, RM-ANOVA). Also, the MINT+TMR group improved by 5.0 \pm 1.4 s (mean \pm SE) on the WMFT from baseline to week 6 (paired t-test, p=0.005), exceeding the minimal clinically important difference of 1.5 seconds. In contrast, the MINT+sham group showed a non-significant trend of 2.3 \pm 1.4 s (p=0.09). The between-group difference in improvement is not quite significant (p=0.07, t-test). MINT+TMR participants also exhibited a trend toward greater improvement in reaching range of motion compared to MINT+sham.

These preliminary findings suggest that TMR may enhance motor learning after stroke, which potentially could improve MINT and other types of neurorehabilitation for stroke survivors.

<u>2-E-67 - Residual Corticospinal Tract (CST) projections engage polysynaptic circuits to sculpt spinal cord</u> <u>stimulation (SCS) for fine motor control post-stroke</u>

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Fine motor control—and thus stroke recovery—is thought to rely on residual monosynaptic connections between the CST and motoneurons. Based on this, SCS is widely assumed to improve volitional motor control in motor disorders (e.g. stroke or spinal cord injury) by increasing motoneuron excitability, thereby facilitating degraded CST fibers. Our findings challenge this assumption. Instead, we demonstrate residual CST projections primarily engage polysynaptic spinal circuits to regulate post-stroke motor control. Moreover, we show that the CST modulates SCS transmission via these pathways, acting presynaptically to the motoneuron and dynamically modulating afferent and interneuron activity to generate functionally relevant motor output.

SCS activates large-diameter sensory afferents, generating la-mediated excitatory postsynaptic potentials (EPSPs) in motoneurons. At 40-60Hz—frequencies optimal for motor recovery—SCS should induce severe rate-dependent depression (RDD) of Ia-EPSPs. However, voluntary contraction could counteract RDD. Additionally, when applying low (5hz) and functional (40-60hz) frequency SCS during passive elbow stretch, reflex response amplitudes were highly dependent on joint angle indicating proprioceptive regulation of spinal excitability. In contrast, during active motion, these SCS-evoked reflexes were further facilitated or inhibited based on task demands (i.e., concentric vs. eccentric), indicating that residual supraspinal projections dynamically shape how SCS engages spinal circuits, beyond basic spinal processing.

To directly examine CST-SCS interplay, we applied a paired-pulse transcranial magnetic stimulation (TMS) paradigm, varying the inter-stimulus interval (ISI) between TMS and SCS. Motor responses were most potentiated when TMS preceded SCS, particularly at long (~100ms) ISIs, suggesting presynaptic facilitation of Ia inputs rather than simple motoneuron summation. Notably, this effect persisted even in MEP- participants, indicating that functionally "silent" CST projections still regulate spinal activity in stroke patients, just not via the monosynaptic CST-motoneuron connection. Motor unit decomposition during TMS revealed that Ia-EPSPs ended before peak ISI potentiation, reinforcing a presynaptic gating mechanism. No pattern was evident when SCS preceded TMS (e.g. SCS did not facilitate TMS).

Functionally, CST engagement of polysynaptic circuits is critical for improved dexterous control. For example, even when SCS failed to increase maximal force output, it consistently improved accuracy in isometric force-tracing tasks, refining agonist muscle activation—sometimes even reducing overall EMG

power. These results suggest that SCS is most effective in dexterity-based tasks, where CST control is predominant. Rather than amplifying weak supraspinal signals, SCS effects are selectively shaped by CST projections pre-synaptic to the motoneuron, underscoring the importance of polysynaptic pathways in functional recovery.

F – Adaptation and Plasticity in Motor Control

<u>2-F-68 - Neural mechanisms of target updating during naturalistic reach-to-grasp actions: insights from</u> <u>a novel motion tracking setup for fMRI experiments</u>

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<u>Details</u>

Neuroimaging research on motor control faces methodological challenges in simulating real-life scenarios. fMRI studies on the topic often employ oversimplified, impoverished experimental paradigms, with static environmental stimuli and absent or constrained visual feedback of one's moving limbs. Here, we investigated the neural correlates of reach-to-grasp movement corrections following social and non-social cues using a novel motion-tracking setup designed for fMRI experiments (MOTUM).

MOTUM consists of an MR-compatible glove tracking flexion and extension movements of the righthand fingers, and an optic motion capture system based on MR-compatible cameras used to track limb (here, right forearm and wrist) movements. Motion kinematic data are then used to animate a humanoid avatar in first-person perspective, with visual output finally presented through a binocular MR-compatible headset providing an immersive experience.

We employed MOTUM in a paradigm where 24 right-handed healthy volunteers grasped either the narrow or wide part of a bottle-shaped 3D object through a precision or power grip, respectively. Grip type was cued either by a light appearing on either part of the bottle (non-social cue) or by the behavior of a partner avatar facing the participants and performing power or precision grasp (social cue). In 33% of trials, the target was updated after movement onset - either through a sudden light switch or a change in the partner's trajectory and grip type -, requiring the participants to adjust their movement on the fly. The appearance and eventual switch of the light were timed to match the partner's movement onset and trajectory change, ensuring comparable temporal dynamics across social and non-social cues.

Imaging data were analyzed using fMRIprep and SPM12. The amount of hand, arm, and head motion was estimated at each timepoint and entered as confound regressors in the GLM to control for motion artifacts.

The change of trajectory following the target update in the non-social cue resulted in enhanced activation of bilateral reaching parietal areas, the ventral and dorsal premotor cortex, supramarginal gyrus (SMG), and left cerebellum, primary motor (M1) and somatosensory cortex. In contrast, trajectory changes in response to the partner's behavior heightened activity in the bilateral caudal and posterior cingulate cortex/precuneus, the left M1, and the right SMG, Extrastriate and Fusiform Body Area.

Our findings highlight SMG as a key hub for detecting and correcting sensorimotor errors, hence being critical for monitoring and switching motor plans. We speculate that this area interplays with different nodes of the parieto-frontal reach-to-grasp circuit and the action observation network to unexpectedly

adapt motor plans in individual and social contexts, respectively. Methodologically, MOTUM represents a promising tool for neuroimaging research, offering an innovative approach to studying sensorimotor control and beyond.

2-F-69 - Different timescales of human sensorimotor adaptation to gravitational changes: evidence from parabolic flights

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<u>Details</u>

The role of gravity in human motor control is well established, but how the central nervous system adapts to gravitational changes to perform complex movements remains poorly understood. While previous research has primarily focused on weightlessness conditions simulating microgravity environments for space missions, this study explored the distinct effects of both microgravity and hypergravity on the neuromuscular control of whole-body reaching movements compared to normal gravity. Nine participants performed reaching movements toward visual targets during parabolic flight maneuvers, enabling analysis of sensorimotor planning and control across different gravity levels. Results revealed that in microgravity, participants adjusted their whole-body kinematics and muscle activity, achieving arm-reaching accuracy comparable to normogravity. Conversely, in hypergravity, systematic undershooting occurred, likely due to insufficient reorganization of muscle activations. To evaluate the efficiency of online control mechanisms, unexpected mechanical perturbations were introduced at movement onset. Despite the gravitational changes, muscular responses to these perturbations remained consistent, indicating that online feedback control was preserved. However, the marked reach errors in hypergravity suggest that fast feedback mechanisms could not offset the absence of effective control reorganization. These findings highlight that hypergravity poses a unique challenge to the human sensorimotor system, potentially disrupting internal models of limb dynamics, requiring further investigation to understand its long-term effects.

2-F-70 - The past and present influence of reinforcement on explicit and implicit error corrections

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Unlike a novice, a professional tennis player is unlikely to drastically change their serve following a failure. Past work in sensorimotor adaptation shows an interplay between reinforcement (i.e., success or failure) and error corrections. Yet it remains unknown how past reinforcement acts to modulate implicit and explicit error corrections. Here we test the notion that a history of reinforcement influences implicit and explicit error corrections.

Participants began in a start position and were instructed to reach through a target, without vision of their hand. They were told if they hit the target they would receive reinforcement feedback (target colour change, pleasant sound, monetary reward). Unknown to participants, we manipulated the probability of receiving reinforcement feedback to control the long-term and short-term reinforcement

history. To control long-term history, different groups of participants experienced either 20% or 80% probability of reinforcement. To control short-term history, we pseudorandomly interleaved fixed reinforcement schedules for two successive trials (i.e., success then success, or success then failure). Error clamps were used to examine the influence of reinforcement history on error corrections. During an error clamp, a cursor was presented as the participant's hand passed by the target. Unknown to the participant, the cursor was a set distance to the left or right of the target. Error correction was calculated as the hand location changed from the clamp trial to the following trial.

In Experiment 1, participants could respond to error clamps by using either explicit (conscious) and or implicit (unconscious) error corrections. Our results showed an influence of long-term reinforcement history, but not short-term reinforcement history. Specifically, participants that experienced 20% reinforcement feedback made larger error corrections than those experiencing 80% reinforcement feedback (p = 0.010). That is, they would change behaviour when they had been less successful. These error corrections could have been the result of either explicit or implicit processes. In Experiment 2, we isolated the potential role of implicit error corrections by instructing participants to explicitly ignore the error clamps. We found no influence of long-term (p = 0.574) or short-term (p = 0.574) 0.576) reinforcement history on implicit error corrections. In a third experiment, we examined the influence of current (present) reinforcement feedback on implicit error corrections. Participants pseudorandomly received reinforcement or no reinforcement, while simultaneously experiencing an error clamp provided within the bounds of the target. We found that reinforcement feedback led to reduced implicit error corrections (p = 0.008). Collectively, these results suggest that past reinforcement history influences explicit error corrections, and only present reinforcement feedback influences implicit error corrections.

2-F-71 - TMS-based neurofeedback facilitates motor imagery of different hand actions

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Details

Introduction: Non-invasive brain-computer interfaces (BCIs) enable users to modulate brain activity in a goal-directed manner. Most non-invasive BCIs can decode only gross movements but many daily tasks require finer finger and hand control. We developed a novel BCI using motor imagery (MI) and transcranial magnetic stimulation (TMS)-based neurofeedback (NF) training to reinforce representations of complex hand actions in the brain. This proof-of-concept study investigates the utility of this BCI for training hand function via MI.

Methods: 12 participants (6 males, mean age 32.0 ± 2.7 [SD] years) completed 4 sessions of TMS-based NF training focusing on 3 hand actions (holding a bottle, turning a key, and opening the hand). The first session involved motor execution (ME), followed by 3 motor imagery (MI) sessions. The ME session comprised 4 blocks (2 blocks per hand, counterbalanced across participants). The MI session comprised 4 blocks: 1 without NF and 3 with NF using the right hand. An additional block without NF was added at the end of the 4th session to assess the learning effect. A personalized, adaptive support vector machine (SVM) ensemble was used for NF during the training, in which a classifier was trained using right-hand ME, left-hand ME, and every MI block data to classify upcoming MI trials and provide feedback accordingly.

We chose average classification accuracy as an outcome measure to gauge the training effect. Blockwise average classification accuracy was derived from an SVM classifier with leave-one trial-out crossvalidation.

Results: To evaluate the learning effect, we used a linear mixed-effect model with MI without NF data and noted that the accuracy of the final MI without NF block (60.5%) showed nearly significant improvement compared to the first block (53.3%; $\beta = 0.091$, $t_{33} = 1.974$, p = 0.057). To investigate if the average decoding accuracy of 9 MI+NF blocks increased over time, we used another linear mixed-effect model and found that Session 3 accuracy (59.3%) was significantly higher than Session 2 (53.3%, $\beta = -0.080$, $t_{88} = -3.208$, p = 0.006) and Session 4 accuracy (58.2%) was marginally significantly higher than Session 2 ($\beta = -0.060$, $t_{88} = -2.421$, p = 0.053).

Conclusions: We developed and tested a novel, personalized, and adaptive MI and TMS-based BCI for complex hand actions. Our findings suggest that healthy adults could modulate brain activities for complex hand actions with the guidance of NF. This demonstrates that TMS-based BCI could be used for hand function training in individuals who are unable to produce overt motor output.

<u>2-F-72 - Dissociating motor and semantic representations in sensorimotor cortex: insights from ablebodied and amputee participants</u>

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<u>Details</u>

The primary motor cortex (M1) is traditionally associated with motor control but also has a role in semantic processing. Previous findings indicate that the sensorimotor representation of the hand persists even years after amputation, raising critical questions about the nature and mechanisms of this maintained information. We hypothesized that the rich semantic associations of daily actions and interactions with the world contribute to stabilizing S1/M1 despite the absence of direct input/output. Alternatively, homeostatic mechanisms may preserve the representation once it develops, regardless of experience.

To investigate these possibilities, we conducted an fMRI study with 20 able-bodied participants and one transradial amputee, examining BOLD activity while they performed hand gestures to interact with various liquid containers. These objects differed in motor demands and semantic associations as well as the intentional context of the actions. Additionally, we recorded hand kinematics using markerless tracking and muscle activity via HD–EMG.

Our primary objective was to characterize the information content in S1/M1. Using representational similarity analysis, we compared S1/M1 representational structure (pairwise multivoxel pattern dissimilarity across all possible objects) with representations of regions associated with action planning (pre-motor cortex), body representation (extrastriate body area), language processing (BA44-BA45 and angular gyrus). We further included an external semantic model (large language model), kinematic model (from hand tracking), and muscle model (from HD-EMG) to assess the representational structure of actions.

In able-bodied participants, S1/M1 representational structure exhibited strong correlations with the kinematic model and premotor activity patterns, and to a lesser extent with the muscle model. Unexpectedly, we found a robust correlation between S1/M1 activity and the semantic model, which was statistically stronger than the relationship of S1/M1 with the semantics brain areas.

Next, we compared these results to our case study amputee. In the deprived S1/M1, we observed a dramatic decrease in kinematic information representation. However, EMG-related information remained comparable to controls, as well as correlations with representation structures found in the premotor cortex. These indicate that while kinematic information was lost, the motor plan and outcome are still maintained in the deprived cortex. Notably, the semantic representations were fully maintained, despite the reduction in kinematic information.

By being able to dissociate muscle, kinematic and semantic contributions to S1/M1, our findings provide evidence that M1 encodes non-movement-related information during executed grasping actions. Future work will expand our sample to include more amputees and apply whole-brain searchlight analyses to further elucidate the interplay between sensorimotor and semantic representations in the human brain.

2-F-73 - The role of Thalamic Neuromodulation in sensorimotor adaptation

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<u>Details</u>

The thalamus, a deep-seated relay hub in the human brain, plays a pivotal role in regulating sensorimotor processes. Despite its critical function, its contributions to sensorimotor adaptation learning remain underexplored, due to the challenges posed by its location deep in the brain. This study investigates the sensory thalamus' role in modulating limb movements and adapting to applied perturbations. We applied transcranial focused ultrasound stimulation (tFUS) to induce neuroplastic changes in the ventroposterior lateral nucleus of 50 healthy individuals (25 active, 25 sham), using personalized stimulation parameters. Following tFUS, participants performed a center-out reaching task with a cursor on a display. To assess visuomotor adaptation, we introduced a 30-degree counterclockwise rotation to the cursor, requiring participants to adjust their motor response. After initial adaptation, the rotation was reversed clockwise, followed by a phase without visual feedback. tFUS significantly reduced thalamic sensory-evoked potentials (SEPs) and alpha-band oscillations while increasing gamma-band activity in the prefrontal cortex, with these effects persisting for up to 20 minutes post-stimulation. Notably, tFUS enhanced both implicit and explicit components of visuomotor adaptation compared to sham stimulation. These performance gains were likely driven by a reduction in thalamic alpha band oscillations, suggesting that diminished sensory gating permitted more unfiltered sensory input to reach the cortex, thereby facilitating faster implicit error-based learning strategies. Simultaneously, increased prefrontal gamma-band activity indicated enhacned cortical processing, likely supporting explicit learning and further contributing to overall task performance improvements.

2-F-74 - Humans adapt their perception of external sensory stimuli during split-belt walking

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Details

The human motor system adapts our actions to counteract changes in the environment (e.g., walking on different terrains) or our bodies (e.g., growth). Motor control relies on sensory information to achieve motor adaptation by contrasting expected and actual sensory consequences of movements. While the adaptation of motor outputs is well-documented, less is known about sensory adaptation and its relationship to motor output adaptation in walking. Previous studies have assessed sensory adaptation through active perception tasks, where participants reported perceived speed differences between their legs.

We hypothesized that perception of leg speed differences would change after a locomotor adaptation protocol, and that this perceptual adaptation correlates positively with motor adaptation. Perception of leg speed differences was measured in young individuals (n=5, 23±3 years old, 2 females) using twoalternative forced choice tasks during split-belt walking, where we maintained a 500mm/s difference between the legs. At each perceptual trial, participants had up to 8 seconds to indicate which leg was perceived as slower while experiencing smaller speed differences ranging between 50 and 450 mm/s. Each of the 9 speed differences was repeated 10 times.

We estimated the point of subjective equality (PSE), which is the stimulus size (i.e., leg speed difference) at which participants perceive both legs to move at the same speed, using a generalized linear mixed model. As anticipated, we observed a significant change in PSE from 0.6±23.7mm/s during baseline

walking to 277.2±24.9mm/s at the end of the split-belt adaptation period (mean±std; $p = 1.8x10^{-17}$). This indicates that participants adapted their perception of leg speed symmetry to 55% of the 500mm/s difference experienced during adaptation. The sustained split-belt perturbation not only adapted participants' movements but also altered their perceptual bias, with a larger effect than previously reported.

To investigate whether perceptual and motor adaptation arise from the same process, we correlated perceptual adaptation with motor aftereffects, defined as changes in step length asymmetry (i.e., differences in step lengths) during post-adaptation compared to baseline. We expected that individuals exhibiting greater PSE changes would also have larger motor aftereffects. However, no statistically significant correlation was found (p=0.27), contrasting with findings from upper-limb adaptation studies. Taken together, our results demonstrate that people adapt their perception of external stimuli inducing movement adaptation during split-belt walking. However, different processes may contribute to perceptual adaptation and motor aftereffects in walking. For instance, feedback and feedforward processes might play distinct roles: both contribute to motor adaptation, whereas only feedforward processes contribute to perceptual adaptation. This distinction will be addressed in future studies.

2-F-75 - Action repertoire as context for motor memory

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<u>Details</u>

When interacting with an object, we select a specific action from multiple possible action patterns. For example, the action patterns used to manipulate a hammer and pliers differ, reflecting how objects

afford distinct sets of possible actions. This pattern can be termed as an action repertoire. In this study, we examined whether differences in action repertoires can serve as contextual cues for switching motor memory. Participants performed 8 cm center-out reaching movements toward five possible targets positioned 45° apart (0°, 45°, 90°, 135°, and 180°). At the start of each trial, three targets appeared. After 1.5 to 1.9 sec, two targets disappeared, and participants reached toward the remaining one. The three-target sets were presented in either a narrow distribution (45°, 90°, 135°) or a wide distribution (0°, 90°, 180°), with each target associated with a distinct visual shape (triangle or square). Each movement distribution was assigned either clockwise (CW) or counterclockwise (CCW) force-field perturbation, and learning was assessed by evaluating force compensation levels during error-clamp trials. A key feature of this design is that the 90° reaching movement was shared between the two distributions. If differences in movement distribution—representing action repertoire—function as a contextual cue for motor memory, participants should be able to learn two opposing force fields, even when reaching to the same 90° direction. Participants successfully compensated for the perturbation in non-overlapping reaching directions (p < 0.001). More importantly, even for the 90° direction, they produced forces aligned with the movement distribution assigned to the trial (p < 0.001). Furthermore, when the association between visual features (triangle and square) and movement distributions (narrow and wide) was occasionally reversed, the learned resisting force was attenuated (p < 0.01), suggesting that visual cues interact with force-field learning and movement distribution. These findings demonstrate that motor memory can be categorized based on differences in potential action patterns. Moreover, the contextual "meaning" of visual features for action control may emerge through their association with specific action repertoires.

<u>2-F-76 - Early learning transitions from offline to online with task simplicity and speed, unveiling a</u> working memory contribution to skill proficiency

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Details

Early learning of a challenging skill evolves over periods of offline wakeful rest rather than online practice [1]. After early learning, skill performance plateaus. After plateau, periods of high initial performance during practice are interrupted by skill drops (i.e. - micro-online drop) [2,3]. The most prevalent interpretation of post-plateau micro-online drops has been that they reflect motor slowing resulting from accumulating fatigue with repetitive typing [1,4,5]. An alternative explanation however is that these micro-online drops reflect limits of a working memory (WM) buffer [6,7,8] engaged in holding individual actions in the correct order prior to their execution [9,10].

Activities of daily living are comprised of sequential skills that vary in difficulty, which describes the overall effort needed to perform a task [11]. The difficulty level of a skill is reflected in its speed-accuracy characteristics (e.g. –easier skills are usually performed faster), and is influenced by the sequence complexity, and biomechanical [12] and neural representation characteristics of the involved effectors (e.g. – surround inhibition between finger representations in M1 that constrain individuated movement) [13]. Manipulating skill difficulty could help disambiguate the influence of motor fatigue and working memory limits on early learning and post-plateau performance dynamics [7].

We investigated these dynamics by developing a difficulty index (DI) for 6-item sequences based upon independent keypress transition time (KTT) data acquired for all possible keypress pairs (n=16). We tested four groups of healthy subjects (n=1467), each of which learned a different skill sequence with

DIs ranging from very easy to very difficult. We found that early learning performance gains accumulate during rest for more difficult skills and during practice easier skills. Thus, early learning transitions from micro-offline for slow difficult skills to micro-online for faster, easier (and thus, more fatiguing) skills.

Micro-online drops observed during post-plateau trials were more prominent for slower, difficult skills. The average number of keypresses performed preceding micro-online drops increased with skill simplicity (Pearson's r=0.38, p<0.001). Interestingly, the number of keypresses prior to micro-online drops increased as training progressed (Very Easy, r=0.89, p<0.001; Easy, r=0.64, p=0.002; Hard, r=0.71, p<0.001; Very Hard, r=0.67, p=0.001) and clustered within 5-7 keypress chunks for all difficulty groups, reminiscent of Miller's working memory rule of 7+2 [14]. This finding is consistent with a working memory capacity limit triggering micro-online drops as opposed to fatigue.

We conclude that (1) early skill learning transitions from offline to online with skill simplicity and speed, (2) micro-offline early skill learning is inconsistent with a motor fatigue origin, and (3) post-plateau micro-online drops are better explained by storage limits of a working memory buffer than by motor fatigue dynamics.

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<u>2-F-77 - Overcoming the limits of motor performance by covert manipulation of feedback on the performance</u>

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<u>Details</u>

An urgent situation or pressured environment often makes people perform beyond or below their ordinary performance. These examples suggest that people implicitly set the limits on their own performance depending on contexts. In the field of motor control, people tend to adjust their performance in response to feedback obtained during a motor task. The current study demonstrated that the performance can be changed by unwittingly manipulated feedback on one's performance during a force exertion. When the feedback is manipulated to underrepresent the actual force, the exerted force went beyond the personal limit.

Fourteen healthy adults (27.3±4.3 yr) were asked to apply their force on a pinching device with the thumb and index fingers for 5 seconds while a time-series of the applied force was displayed on a screen in real time. Each participant exerted the maximum force and 50% of their maximum force on a subjective scale in 3 trials each. Each trial was assigned to one of the three types of feedback unwittingly to the participants: genuine feedback (no manipulation), upward feedback (gradually increased during the second half of each trial), or downward feedback (gradually decreased during the second half of each trial). We compared the average and variance of the applied force across the period (the first vs. second half of the trials) by a paired t-test.

In both tasks, the average force in the second half was significantly lager with the downwards feedback (average increase of 7.9% in maximum force and 11.9% in 50% force) and smaller with the upwards feedback (average decrease of 7.0% in maximum force and 8.8% in 50% force) compared to that in the first half. These results suggest that the participants' under- or over-estimated their own force due to the unwittingly manipulated feedback, which in turn increased or decreased the applied force. There was no systematic difference in variance of the force across the periods.

Our findings suggest that the limit of people's motor performance (i.e., force exertion) can be changed due to changes in the perception of their performance based on the covert manipulation of feedback. With the appropriate use, such feedback manipulation may contribute to the improvement of motor performance and promotion of learning and skill aquation in various sports fields. On the other hand, it has theoretical implications on how the brain controls its own limit in performance.

2-F-78 - Whole body motor adaptation in goldfish using fish operated vehicle

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Details

Motor adaptation is a key tool for understanding the mechanisms of the sensory motor loop. We explored motor adaptation in fish using a Fish Operated Vehicle (FOV). FOV is a robot which can be operated by trained fish. Fish use their position and orientation in the water tank of the FOV to control the movement of the robot. Our data show that goldfish can learn to operate the FOV and adapt to perturbations of the steering. Multiple fish demonstrate both adaptations to perturbed steering period. Preliminary data indicate that fish exhibit no clear saving when adapting a second time to the same perturbation. And there is a potential negative correlation between the learning rates of this two stages

2-F-79 - Persistence of resting-state functional connectivity changes attributable to novel sensorimotor learning and retention

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<u>Details</u>

Learning a new motor skill alters the architecture of brain connectivity. However, it remains unclear how durable these changes are and what their relationship is to the retention of the motor skill itself. Here we used functional magnetic resonance imaging (fMRI) to (i) identify changes in resting-state functional connectivity (RS-FC) that show relationships with behavioral measures of novel sensorimotor learning and retention, and then to (ii) determine whether those observed changes persist across scanning sessions on back-to-back days. We used a novel paradigm in which 25 healthy subjects learned to perform reaching movements with an MR-compatible joystick at different angles in a 2D workspace to create acoustical targets. At the end of each reaching movement, participants received auditory feedback corresponding to the sound associated with the angle that they moved in. Motor performance was quantified on each trial as the absolute angular distance from the target reach movement angle. On day 1, participants completed training (with feedback) and pre- and post-learning tests (without feedback). On day 2, participants completed a retention test (without feedback), which reactivated the brain network involved in performing the task. We collected fMRI data while participants performed the task to identify areas in which the amount of activation scaled with learning. We then examined changes in RS-FC observed at multiple time points after training. The behavioral results showed that participants incrementally produced movements with smaller angular errors, indicative of learning. Furthermore,

this learning was largely retained on day 2. In analyses to date, a cluster in the superior parietal lobule was observed during the task to show increased activation for participants who displayed greater performance gains on day 1. This cluster was then used as a seed in a whole-brain RS-FC analysis. We compared RS-FC with this seed prior to and after training on day 1 to assess learning-related changes. We also acquired two more resting-state scans on day 2 to assess retention-related changes in connectivity, one prior to the retention test, the other after the retention test. We identified a network involving motor and auditory cortices whose activation was related to learning measures on day 1. We also identified a separate network involving motor, auditory, and somatosensory cortices whose activation was related to retention-related changes in connectivity were detectable even without participants having performed any movements (i.e., both prior to and after the retention test on day 2). Thus, changes in RS-FC that are attributable to motor learning and retention persist overnight and across scans and do not require network reactivation through motor practice to be elicited.

Highlights of submission:

- 1. Single-session motor learning results in retention-related changes to resting-state networks.
- 2. Retention-related changes persist overnight and are detectable in the absence of overt movement.
- 3. Subsequent motor practice is not required to elicit a RS network linked to retention.

Justification statement: Research on training-induced plasticity in motor and sensory systems has shown changes in resting-state sensorimotor networks linked to motor learning and retention. Here we show that those changes in RS-FC persist overnight and across scanning sessions, regardless of whether participants reactivate the affiliated neural networks through overt motor practice.

2-F-80 - Hand dominance does not influence motor adaptation

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Details

While hand dominance clearly modulates motor control, its impact on motor adaptation—the process of correcting for errors through feedback and practice—remains controversial: some studies show greater adaptation in the dominant hand, others find no difference, and some report the opposite pattern.

To address this controversy, we conducted a meta-analysis on the effect of hand dominance in motor adaptation. We included studies that directly compared adaptation between the dominant and non-dominant hands and reported at least one measure of adaptation. A total of 25 studies (29 datasets) met our criteria, spanning 2002–2023, covering 15 visuomotor rotation, 5 force-field, 4 prism, and 1 weight adaptation task. On average, each study tested only 12 (SD = 7.65) participants per group and comprising little statistical power in detecting group differences (power = 0.09 [0.08, 0.18], with alpha = 0.05). Notably, all but one study focused exclusively on right-handers.

Although results varied across studies (early adaptation, $I^2=76\%$, p< 0.0001; late adaptation $I^2=99\%$, p< .0001, and after-effects phase $I^2=66\%$, p= 0.0004), we found no evidence that hand dominance affects motor adaptation. Adaptation was similar between hands during early

adaptation (early g=0.11, 95% CI [-0.23, 0.45]), late adaptation (g= -0.12, 95% CI [-0.53, 0.29]), and aftereffect phases (g= -0.18, 95% CI [-0.53, 0.16]). Across the three phases, there was a sign of publication bias only in the late adaptation phase ($X^2(1)$ =6.16, p=0.01).

In summary, we failed to find any evidence that motor adaptation differs between the dominant and non-dominant hand. Our future work will address key gaps in the literature by increasing sample size, including both left- and right-handers, and using targeted learning assays to examine whether hand dominance and handedness impact distinct implicit/explicit learning processes supporting motor adaptation.

2-F-81 - No evidence for facilitation of finger motor sequence learning from passive robotic movement

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Details

Robotic devices allow for detailed investigation into the conditions where passive movement can induce motor learning. Evidence for robotic facilitation of motor learning involves tasks that depend on proprioception: reaching in a specific direction or drawing a perfect circle. For tasks with smaller movements such as sequential button pressing, few conclusive results have been presented. Here, we aimed to provide a thorough analysis of the potential of motor learning facilitation for small finger movements through a set of motor sequence learning experiments. We developed a keyboard-like robot that can be used to both record and replay movements across all 10 fingers in a small range of motion (approximately 10 degrees of rotation). Through a predictive control algorithm, we were able to synchronize the passive movement (i.e. from one hand to the other) without any apparent perceptual delay. An initial set of experiments followed an intermanual transfer paradigm with robotic mirroring. Participants learned a set of 9-button sequences over 2 days with the right hand, then were tested with the left hand on Day 3. There were 3 training conditions: instantaneous physical mirroring, trial-delayed physical mirroring, or no mirroring. On Day 3, we found no significant difference between training conditions on left hand performance, indicating that passive movement of the left hand did not facilitate motor sequence learning beyond the intermanual transfer effect from right hand movements during training. We identified two possible confounds: first, we aimed to enhance intermanual transfer, which may override any passive movement benefit; and second, no active left-hand movement occurred during Days 1-2, which may be necessary to realize passive movement benefits. The next set of experiments involved only the left hand on a single day: participants performed a sequence memorization task immediately followed by a sequence execution task. Sequence memorization consisted of a visual replay of a sequence execution followed by a 2-alternative forced choice selection of the sequence element in a random position. Half of the sequence visualizations were also accompanied by a physical replay sourced from movements in previous experiments. In the sequence execution post-test, we found no difference in performance for sequences that were physically enhanced compared to those that were purely visual. Our results show that passive robotic movement does not significantly facilitate motor sequence learning with small finger movements, across several conditions: same- or multi-day learning, intermanual transfer or unimanual training, and instantaneous or delayed movement replay. Future work will aim to determine whether sequence learning tasks with a larger range of finger motion, and therefore greater proprioceptive importance, are influenced by passive robotic training.

2-F-82 - How memory reactivation influences motor skill retention and interlimb generalization

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<u>Details</u>

Retention and generalization are considered hallmark features of newly learned motor skills in humans. Such retention and generalization can be influenced by interventions that affect memory consolidation. One way to influence memory consolidation is by brief reactivation of the underlying memory. Such effects of memory reactivation have been widely studied in animal models, and lately, its efficiency has been demonstrated in humans in the context of motor sequence learning. However, whether such reactivation can influence retention and generalization of a newly acquired reaching skill in humans is unknown. Our goal here is to specifically understand the effects of a brief memory reactivation session on subsequent motor skill performances (by testing for intralimb retention and interlimb generalization). Based on the limited literature, we hypothesized that skill memory reactivation will strengthen the newly consolidated skill memory and thereby enhance both retention and generalization test performances.

To study this, we recruited young healthy right-handed participants (n=72) who performed a novel motor skill task- fast and accurate reaching movements to one of eight randomly presented target circles on a digitizing tablet. Participants received visual feedback and a numeric score indicating 'motor error' at the end of each movement trial and were asked to reduce this error to successfully learn the skill task. The study involved three session- a training session (160 trials separated in 20 bins of reaching movements using right arm on day-1), a brief reactivation session (2 bins with right arm on day-2 or 3) and finally, a test session (20 bins with right or left arm on day-3). Following training on day-1, participants were divided into four groups: i) Retention with Reactivation (Right arm used for all three sessions on all three days), ii) Generalization with Reactivation (right arm for day-1 training and day-2 reactivation, left arm for day-3 test), and iv) Generalization with Delayed Reactivation (right arm for day-1 training and day-3 reactivation, left arm for day-3 test, allowing us to assess the temporal effect of reactivation on testing).

We quantified learning as a reduction in motor error from the first to last bin of training session on day-1. Next, we compared groups on the reactivation performance. Finally, to quantify retention and generalization, we expressed first bin of day-3 test session with respect to first bin of training and compared across groups. Based on our ongoing statistical analyses, we found significant learning in all groups with a comparable performance during reactivation, which we expected. Next, we found a significant retention and interlimb generalization in the respective groups, with no specific effect of the brief reactivation. However, upon classifying subjects into 'high' versus 'low' learners (based on their training performance on day-1), our preliminary findings indicate that skill memory reactivation was beneficial for interlimb generalization for low learners only. No such benefit was observed for high learners or in the context of retention. These findings indicate that a brief reactivation may facilitate interlimb generalization to individuals with lower amount of learning during the training session.

2-F-83 - A pilot study on the impact of proprioception on referred control

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<u>Details</u>

Human movement augmentation by transfer (also known as "referred control") is a human-machine interfacing paradigm in which task-extrinsic neural degrees of freedom (DoFs) are used as control inputs to task-essential robotic DoFs [Eden, Nat. Commun. 2022]. This idea has gained traction in the field in recent years, but individuals have not yet been able to accurately and reliably control referred devices [Parietti, ICRA, 2017]. These mechatronic referred control challenges are juxtaposed by the success of tendon transfers, a form of biological referred control where a tendon is surgically rerouted from its native track to a recipient track where activation of the muscle leads to a new physical function in the body. This procedure commonly restores function as the individual learns to use their rerouted functional motor pathways [Ochi, J Hand Surg., 2012]. Due to this success, we believe native proprioceptive feedback is important in referred control performance and designed an experiment to test that.

In this pilot experiment, surface electrodes were placed on two sets of antagonistic muscle pairs on the right side of three able-bodied participants. EMG from the biceps and triceps controlled one virtual dynamic joint [Au, ICRA, 2005] and EMG from the pectoralis major and middle trapezius controlled another. Participants were shown a virtual interface with target joint positions and were asked to try to match and hold the positions. Success was defined as both virtual joint positions being within 15° of their targets for 1 second within a 1.2 second window. Participants were given 20 seconds for each trial followed by 5 seconds rest.

We evaluated three different forms of proprioceptive feedback: one where individuals could freely move their arm ("free space"), one where their arm was held still in a neutral position by a device ("isometric"), and one where their arm was moved through random positions by a device ("errant feedback") while trying to complete the virtual task. We hypothesized that free space control would result in participants completing the task with the highest success rate and in the shortest amount of time as it would give the individual the most task-relevant proprioceptive feedback.

On average individuals performed with the highest success rate (Supplemental Figure 1) and completed successful trials quickest in the free space condition (Supplemental Figure 2). Paired t-tests between conditions showed a significant difference only between the free space and errant feedback conditions for success rate, however we believe more significant findings may arise as more data are collected. Additionally, it is worth noting that only one participant (denoted in pink) was a novice user of the control and feedback systems. These preliminary results support our hypothesis that free joint position proprioceptive feedback is important in mechatronic referred control.

2-F-84 - Temporal indexing of motor memory

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<u>Details</u>

We are often required to rapidly and automatically select appropriate motor memories in real time – from deciding the exact pressure to apply to a car brake, to retrieving slightly different swing kinematics when trying to hit a baseball. Retrieving appropriate motor memories is facilitated by contextual cues that bridge preparatory and execution phases of movement (Churchland & Shenoy, 2024; Heald et al., 2021). Cues considered in previous research are typically external, such as the spatial goal of a motor

plan, or explicit sensory signals (Sheahan et al., 2016; Avraham et al., 2022; Howard et al., 2013). However, to date, the role of a critical contextual variable – time itself – remains largely unexplored. Here we ask if internally represented temporal intervals can act as effective contextual cues for motor memory.

We designed a visuomotor "dual adaptation" paradigm where humans made reaching movements to a visual target, and experienced a fixed cursor perturbation (+ or -15°), randomly distributed over training. Participants were aware of the clamped feedback and actively ignored it, ensuring implicit learning (Morehead et al., 2017). Critically, we implemented a novel "ready-go" task (Jazayeri & Shadlen, 2015), where each rotation was deterministically coupled to a distinct temporal interval: a fixed delay between a "ready" cue (grey target) and a "go" cue (target turns green) of 500 or 1500 ms. Participants internalized the intervals, showing a reduction in RT over training, even though the intervals were randomly interspersed. Strikingly, we found that the learned delays afforded simultaneous implicit adaptation to the two opposing errors, effectively partitioning the competing motor memories. That is, participants showed distinct reach directions on short versus long delay trials in a manner that compensated for the perturbation associated with each delay. We emphasize that no external information about temporal context was ever given (e.g., a visual timer) – participants had to represent the temporal conditions internally. We then tested "temporal generalization", varying the ready-go interval between the short and long delays in increments of 250 ms (750, 1000, 1250). Participants showed a near linear change in their compensation, with reach kinematics for intermediate delays reflecting a gradual shift in the magnitude and direction of adaptation based on the learned temporal associations from the training phase. These findings suggest that time not only separates motor memories, but also enables generalization across different delay durations in a highly structured fashion.

Our findings suggest that internal time-keeping, perhaps reflected in the dynamics of low-dimensional trajectories in sensorimotor cortex during movement planning (Churchland & Shenoy, 2024), can index motor memories and guide memory retrieval. These results lay the groundwork for further exploration of questions concerning temporal-context-based motor memory.

2-F-85 - Do people only adjust ongoing movements vigorously when it is advantageous to do so?

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Details

When reaching for objects, people's movements are constantly guided by the latest available information about such objects' positions. We previously found in several experiments that the vigour of responses to new information increases during the movement, ensuring that the adjustment is completed at the moment of contact. Here we examine whether this is a general principle, or whether it was a consequence of the design of our experiments making it the best thing to do. To answer this question, we compared the vigour of adjustments in blocks of trials in which targets followed a random walk with the vigour of adjustments in bocks of trials in which the target position varied at random around a fixed position. For the random walk, the latest position is the best estimate of the final position, so making vigorous adjustments can be useful. For random variability around a fixed position, the target's position at any instant is equally informative about the final position, so making vigorous

adjustments in response to the latest information is pointless. In that case, the best estimate of the final position is the average of all the encountered positions. Some participants responded less vigorously in the latter case, but others did not, suggesting that doing so had to be learnt.

2-F-86 - Explicit strategies may emerge discretely, not progressively

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Details

Motor adaptation comprises various processes, including explicit strategies. These are usually assumed to develop progressively, and sometimes to gradually decay again when implicit processes take over. However, while we have seen that a group average time course of the magnitude of explicit strategies indeed looks progressive, in individual participants it does not. First, while overall adaptation and implicit components develop somewhat in all participants, there are usually a few participants without (a reported) explicit strategy - depending on how clear the perturbation is. Then, in those who do develop a strategy, this appears to occur rather suddenly. That is: strategy development seems not to be a progressive process, but is marked by discrete moments of insight. This may be reminiscent of Aha! moments in other cognitive learning processes. Here we show first steps in an attempt to describe explicit motor adaptation as a discrete process.

2-F-87 - Separate motor memories are formed when linked to different reward states

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<u>Details</u>

Previous studies have demonstrated the influence of rewards and punishments on motor learning and control. For example, Galea et al. (2015) found that punishment accelerates learning in a visuomotor rotation task, while reward increases retention. In addition, it has been shown that movement tends to be faster when directed towards rewarding options as opposed to punishing ones (Shadmehr et al., 2019).

In this work, we examine whether rewarding and punishing states can function as contextual cues allowing the separation of two motor memories. In a first experiment, participants (n = 8) made forward movements to a single target and were exposed to two opposing velocity-dependent force fields, which were randomly interleaved across trials. The direction of the field was indicated by the target color which also determined the reward regime. Green/red targets indicated the rewarding/punishing regimes in which the participant won/lost points based on performance. For the rewarding condition the number of points won depended on a exponential of the maximum perpendicular error (MPE) of the movement (100 exp(-k* MPE)). For the loss regime participant lost 100-100 exp(-k* MPE) points. Participants knew that the total accumulated points corresponded to the pay at the end of the experiment. In addition, we displayed a small chart on the screen with the equivalence of total points and dollars throughout the task.

We found that 6 out of 8 subjects showed clear evidence of adaptation to both force fields. In addition, the number of points earned in the rewarding trials increased over time, while the number of lost points in the punishing trials decreased, suggesting that participants aimed to maximize their utility. We compared their performance to a control group (n = 8) that completed the task only in the rewarding state – that is, they were only earning points –, while still indicating the field sign with different target colors. None of the participants in this group showed adaptation to either of the force fields.

In summary, our work suggests the valence of the contextual cues is a key factor to separate motor memories and exemplifies the close interaction between reinforcement learning and motor learning.

<u>2-F-88 - Conscious decision making in visuomotor adaptation: The effects of target selection and pre-</u> planning a movement strategy

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Details

In order to complete everyday tasks, one must engage in decision-making processes related to action selection and movement planning. These decisions often occur unconsciously, even amidst changes in the environment. Across two experiments, we sought to determine the impact of conscious decisionmaking processes on visuomotor adaptation. Specifically, we investigated how decisions regarding target selection and pre-planning a movement strategy influence visuomotor adaptation. In general, participants reached with cursor feedback on a screen that (1) accurately represented their hand motion (aligned cursor), or (2) was rotated 40 degrees clockwise relative to their hand motion (rotated cursor). Following reaches with cursor feedback, the extent of explicit (conscious strategy) and implicit (unconscious) adaptation were assessed using the process dissociation procedure. Participants reached in the absence of cursor feedback when instructed to (1) engage in strategic reaching (i.e., assessment of explicit adaptation) and (2) reach directly to the target (i.e., assessment of implicit adaptation). In Experiment 1, a Choice group (CHO; n = 54) had the opportunity to select the target prior to reaching, while a Yoked group (YOK; n = 54) reached to targets in the sequence selected by the CHO group. In Experiment 2, a Direction group (DIR; n = 18) was asked to report the direction their hand should aim prior to reaching, while the Endpoint group (END; n = 18) was asked to report where their hand should end relative to the target. A Control group (CTL; n = 18) did not provide a report prior to reaching. Analyses of rotated reach training trials indicated no significant differences between the CHO and YOK groups (p>0.096). On the other hand, the DIR and END groups demonstrated greater visuomotor adaptation compared to the CTL group (both p < 0.017). Following rotated reach training, assessment of explicit adaptation indicated that the CHO group displayed greater explicit adaptation compared to the YOK group (p = 0.003). Additionally, analyses indicated that the DIR group displayed significantly greater explicit adaptation compared to the CTL group (p = 0.033), while the END group did not differ from the CTL group (p = 0.150). There was no significant difference in implicit adaptation across all groups (all p >0.841). Together, these findings suggest that engagement in conscious decision making influences the extent to which participants adapt their reaches to a visuomotor rotation. Whether selecting the target to reach to or planning a movement strategy, decision-making processes lead to increased explicit visuomotor adaptation.

G – Theoretical and Computational Motor Control

<u>2-G-89 - The brainstem modulates sensory transmission to primary somatosensory cortex in task-</u> <u>dependent ways</u>

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Details

Background: Cutaneous and muscle proprioceptive mechanoreceptors provide critical sensory information to the primary somatosensory cortex (SI) for voluntary hand function in primates. Textbooks describe the thalamus as the main relay for sensory signals from the spinal cord to SI—although the less known cuneate nucleus (CN) of the brainstem, in fact, relays information from the dorsal root ganglion to the thalamus. Given that the CN is known to modulate haptic signals in the cat, we investigated if it also modulates upper limb cutaneous and muscle proprioceptive signals in primates . Purpose: To test for differential and contextual modulation in the cuneate nucleus on the way to SI during voluntary wrist flexion and extension movements. Methods: We recorded stimulation-evoked local field potentials (SEPs) from the cuneate nucleus (8 electrodes) and the SI (32 electrodes) during stimulation of the sensory (i) deep radial nerve (DR, muscle proprioceptive) and (ii) superficial radial nerve (SR, cutaneous) in during voluntary wrist flexion and extension (Kubota et.al. (2024)). Results: The average SEPs have distinct shapes across subregions of CN and SI, and across tasks. During SR stimulation (cutaneous sensory information), with a larger initial negative peak in SEPs, compared to DR stimulation (muscle proprioceptive sensory information). Novel cross-correlations between CN and SI are lower for DR stimuli and tend to peak after cross-correlations for SR stimuli during both flexion and extension. Conclusion: Lower correlations in DR may suggest that the DR signal is weakly represented in the SI, compared with the SR signal, which is expected because of the subconscious nature of muscle proprioception.

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Reference: Kubota et al (2024) Modulation of somatosensory signal transmission in the primate cuneate nucleus during voluntary hand movement. Cell Reports 43(3).113884.

<u>2-G-90 - Retrieving the structure of probabilistic sequences from the EEG data during the goalkeeper</u> game

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<u>Details</u>

The statistical brain conjecture states that the brain performs statistical inference to retrieve the structure of probabilistic sequences of events. We used the Goalkeeper Game, a computer game developed by NeuroMat (game.numec.prp.usp.br) to test this conjecture. Acting as a goalkeeper, the participant is asked to predict each kick in a sequence of penalties while his/her EEG activity is recorded. The penalty taker's sequence is generated by a probabilistic context tree. We applied the Context Algorithm to the EEG data recorded during the game. The retrieved trees may match (or not) the context tree generating the kicker's choices. In the match case, this indicates that the EEG segments recorded from the goalkeeper during the game display the same dependencies on the past as those of the kicker's sequence. Twenty-six right-handed subjects (12 F, 24 ± 6.61 years) participated in the study. The kicker chooses one of three options at each trial: left, center, or right. These options are referred to as 0, 1, and 2, respectively. Each participant performed 1500 trials (3 blocks of 500 trials). The goalkeeper informed his prediction choice by pressing buttons mapped to 0, 1, and 2 on a keyboard. Each button was addressed to a single finger of the right hand: index (0), middle (1), and ring (2). After the button press a feedback animation showed the outcome of the subject's prediction. Raw EEGs (32 elec., avg ref., ActicHamp, 2.5kHz) were filtered at 1Hz for ICA decomposition. ICLabel was used for artifact removal. The resulting EEG was low-passed in 45 Hz and then downsampled to 256 Hz. The tree estimation was done for each electrode/block/participant, considering EEG segments time-locked to the button press (-300ms to 0ms). The algorithm uses the projective method to reduce the dimensionality of each EEG segment to one, then distributions of the projected EEG segments are compared using the Komolgorov-Smirnov test with a significance level of 5%. A mode context tree was estimated from the set of retrieved trees of each electrode and block. The mode context tree presents the most frequently retrieved contexts on the set of trees. For most electrodes and blocks the mode context tree corresponded to the penalty taker's tree. Furthermore, a distance was calculated from the penalty taker's tree and each block/electrode retrieved tree. We observed a reduction of the overall distance distribution across the blocks for most electrodes which reinforces that the EEG dependencies become more congruent with the penalty taker tree as the subjects move forward from one block to the other.

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2-G-91 - Neuromodulation increases the flexibility of motoneuron control

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<u>Details</u>

Movement requires the careful orchestration of the activity of hundreds of muscles. The force of each individual muscle is determined by the rate-modulated activity of hundreds of innervating spinal motoneurons. An important open question is how flexibly these motoneurons can be controlled by the nervous system. The classic view is that of rigid control: common synaptic inputs are projected to all the motoneurons innervating a muscle (or muscle compartment), providing a one-dimensional control signal. As a result, motoneurons are recruited in an orderly fashion, from smallest to largest. Recent studies, however, suggest that motoneuron control may be more flexible: the recruitment/derecruitment order and correlations between pairs of motoneurons from the same muscle can change both during intracortical microstimulation (Marshall et al., Nature Neuroscience, 2022) and under volitional control (Bräcklein et al., eLife, 2022).

Here, we sought to understand the neural mechanisms underlying these apparent violations of rigid motoneuron control. We hypothesized that such flexibility would originate from the descending neuromodulatory inputs to motoneurons originating from the brainstem. These neuromodulatory inputs can alter motoneuron excitability leading to effective gain changes, and even produce sustained motoneuron firing after cessation of synaptic inputs.

We implemented a biophysical model of a motoneuron pool based on multicompartment Hodgkin-Huxley neurons that received common synaptic inputs along with neuromodulatory and inhibitory inputs. After parameter optimization using large-scale motoneuron recordings (n \sim 130 per subject) from two leg muscles, the model accurately replicated experimental data well ($R^2 = 0.89$). We then combined this model with a proportional-derivative controller that determined the ongoing synaptic input to simulate the online motoneuron control experiments by Bräcklein et al. There, participants performed a two-dimensional cursor control task in which the activity of two motoneurons from the same muscle each controlled cursor position along on axis; importantly, acquiring one of the three targets required decorrelating the activity of these motoneurons. A direct comparison of the same model architecture with and without neuromodulatory inputs confirmed that neuromodulation is necessary and sufficient to decorrelate the activity of motoneuron pairs from the same muscle, leading to deviations from rigid control. Consistent with experimental observations, such flexible control was only achievable for motoneuron pairs with dissimilar biophysical properties, since this is required to exhibit differential responses to neuromodulation. Thus, this work shows that the intrinsic differences in biophysical properties across motoneurons from the same pool, combined with descending neuromodulatory input, can lead to higher dimensional control of muscle output than predicted according to classic views of motoneuron control.

2-G-92 - Changing prior beliefs about other agents directly tunes our sense of agency

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<u>Details</u>

The sense of agency (SOA) originates from the ability of the individual to discriminate between selfmade and other-made actions based on the outflow of motor commands and the inflow of sensory feedback. Specifically, if we consider a Bayesian-based inference framework, self-agency is formed when the observed outcome matches our actions and the high belief that the agent responsible for the outcome is us. Although the idea of Bayesian inference as the basis for the SOA was suggested in the past, there is only limited and indirect evidence for the validity of this model. Here, we aimed to test the model by directly changing the prior belief in the acting agent.

Participants played a virtual game similar to shooting an arrow toward a target using a bow. After familiarizing themselves with the game, they played against a virtual player which also aimed to shoot a second ball toward the same target (from the opposite direction). Participants played against two types of virtual players in a block design (the order was counterbalanced across participants). The first type was the *sharpshooter* virtual player whose shots were distributed accurately around the target (uniform distribution between ± 1.5 cm around the target). The second type was the *amateur* virtual player whose shots were distributed automatic between ± 2.5 and ± 4 cm). In each trial, both players had to shoot their balls toward the target, and the player whose ball was the closest to the target center got points. Once the participant made their shot, we displayed their and the virtual player's hit positions. In 1/3 of the trials, after the participant made their shot, we did not

display the two hit positions, but instead, we displayed a shifted version of the participant's hit position. The shifts were chosen from a discrete uniform distribution between (-3) and (+3), including a zero shift. After showing the landing position, we asked the participant to judge whether the displayed hit position resulted from their own shot or the virtual player's shot.

Participants associated the displayed hit position with the virtual player according to the distribution setting and the nature of the player. Even though the displayed hits during the agency questions were always an outcome of the player shots, participants could mistakenly assign them to the virtual player according to the learned distributions of the amateur or the sharpshooter players. However, we observed a clear shift in the mean of these learned distributions when playing with the sharpshooter and amateur players, with means of 4.36 and 5.8 cm around the target, respectively. These results show the direct effect of elevated prior belief in other-agent actions on the SOA. Moreover, it provides more evidence against a comparator model (such as a forward model) for forming self-agency since such a model is based solely on comparing actions and outcomes without accounting for past experiences.

2-G-93 - I need a break: task similarity's effect on control allocation in motor skill learning

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Details

Learning new motor skills, like playing the piano, is cognitively demanding and often requires frequent breaks to sustain performance. However, breaks are rarely spent idle; instead, we engage in activities like talking, texting, or planning, which still help us recover and return to practice with renewed energy. This raises the question: why do these seemingly unrelated tasks aid recovery and improve performance? Previous work has suggested that training on the same task reduces control through the breakdown of surround inhibition in the somatosensory cortex of antagonist muscles, making movements less efficient and worsening performance. However, other work has suggested that the expected value of control on a task decreases as one repeatedly trains because the opportunity cost to do a different and, potentially, more rewarding task grows over time. This suggests the similarity of the task goal influences the allocation of control. These findings imply that the similarity of the break task to the primary task – in terms of either kinematics or task goal – might influence the allocation of cognitive control. To test these ideas, we employed a modified finger-tapping task with two experimental manipulations. First, we altered the apparent task goal by changing the contextual framing: participants executed a sequence of keypresses to either navigate a virtual maze or play a piano melody, thereby shifting the goal associated with the motor sequence. Second, we manipulated kinematic similarity by switching the hands between the tasks. In addition, we tested several control groups who were required to perform the same task with the same hand and were matched to the test group with respect to the number of sequences executed and/or training time to the test conditions. Our findings reveal that, relative to the control groups, all experimental groups exhibited reduced control allocation during training – measured as the improvement in reaction time from the end of training to the test trials after a 15 minute rest period, a metric which has been previously used to measure the amount of decrease in control allocation in motor skill learning. Our findings suggest that both the similarity in task goal and kinematics contribute to the allocation of control during a task.

2-G-95 - Preserved neural dynamics across arm and brain-controlled movements

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<u>Details</u>

The neuronal tunings in motor cortex have been found to dramatically transit from planning to executing movements. Prevalent dynamical systems view posits that cortical preparatory activity develops toward a movement-specific optimal subspace to set initial states seeding temporal evolution for generating movement. However, most intracortical brain-machine interfaces (iBMIs) relies on continuously converting neural activity to motor variables by fixed decoders, leading to modest performance in speed and smoothness. Thus, intercepting a moving object with brain-control remains a challenge for current iBMI designs, whose neural dynamics and control strategy are profoundly different from naturalistic arm movements. While monkeys manually intercept moving targets, cortical preparatory activity predicts upcoming movement with compensation for sensorimotor delays, inspiring us to design iBMIs generating desired motor program from neural activity in a feedforward manner. Here, we designed a biomimetic iBMI enabling monkeys to initiate neural states leading to a ballistic movement. In preparatory epoch, a computer cursor was visually directed by motor cortical activity raised by monkeys. Once the cursor touched the ring that surrounded the screen center, it was launched radially along a straight trajectory with a bell-shaped speed profile without in-flight correction. After implanting Utah arrays into their motor cortex, we trained two monkeys to intercept a moving target with circular velocity of ±120 deg/s by the brain-controlled cursor. Within few weeks, both monkeys learned to utilize the iBMI to launch the cursor, generating rapid interception of moving targets with a high success rate (>70%) and efficient trajectory. Dimensionality reduction revealed that population activity in brain-controlled trials resembled the dynamical structure observed in the manual interception. Notably, the preferred direction (PD) of neuronal tuning shifted across epochs, particularly before and after the cursor touched the ring (i.e., the preparatory and execution epochs). To characterize PD shifts in the brain-controlled trials, we analyzed population neuronal activity within 100 ms before and 300 ms after the ring-touch event by projecting it onto jPCA space. The neural trajectories exhibited a rotational structure, indicating the preserved neural dynamics in the iBMI control. Apparently, the cortical preparatory activity raised by the monkey served as the initial state, then the subsequent neural states were generated by the dynamical system once the cursor was launched, resulting in the neural transitions and PD shifts. It seems likely that emergent preserved pattern in neural dynamics resulted from feedforward iBMI reflects neural dynamical principle underlying naturalistic motor control at neural circuit level in the absence of muscle activity and biomechanical constraints.

2-G-96 - Phase-dependent primitives in motor adaptation

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Details

The motor system adapts to different environments by forming an internal representation of bodyenvironment dynamics. Traditionally, this representation is thought to be encoded by state-dependent motor primitives, specifically velocity and position (Sing et al., 2009). Here, we show that it is also encoded by phase-dependent motor primitive, where "phase" refers to the temporal progression of movement relative to its overall structure.

In Experiment 1 (N = 16), participants learned to move a cursor 16 cm to a frontal target while experiencing an S-shaped force perturbation that reversed direction between the first and second halves. After learning, we examined its generalization to reaching movements of different distances. Participants performed 8 or 16 cm reaching movements under a clamp channel, which were randomly interleaved within the force perturbation trials of the 16 cm reach, and the forces exerted against the channel were measured. The results showed that the force profile exhibited a similar S-shaped curve for both movement distances. Notably, despite having experienced force perturbation trials, participants exerted not only the experienced rightward force but also an unexperienced leftward force during the 8 cm reach. This finding suggests that motor memory is not strictly tied to movement states such as position and velocity but instead may be encoded in a more abstract, phase-dependent manner.

However, the results of experiment 1 can also be explained by assuming acceleration-dependent primitives. To dissociate the effects of phase and acceleration, experiment 2 employed a double-reach task, in which velocity momentarily dropped to zero at the midpoint. In the follow-through task, participants first moved through a perturbing force field from the start position to a central target and then immediately made a subsequent unperturbed movement to a follow-through target located at 45°. In the lead-in task, they initiated an unperturbed movement from a lead-in starting position located at 45° and made a reach where the force field was applied in the opposite direction to that in the follow-through task. This paradigm allows participants to experience conflicting force field with the same movement (in terms of position, velocity, and acceleration), with the force field direction being associated with the phase (first or second half). Participants learned the conflicting force fields more quickly than when they were associated with different follow-in movement directions (Howard et al., 2015). Furthermore, when participants performed a forward double-reach under an error-clamp condition, the force profile showed opposite directions between the first and second reaches, indicating that motor memory is learned associated with phase. These findings suggest that phase serves as a fundamental temporal axis for encoding motor memory.

2-G-97 - Retrieving the probabilistic structure of the goalkeeper's game in motor evoked potentials

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<u>Details</u>

The neural basis of statistical learning is still unclear. We have investigated the learning of stochastic sequences using a game called the Goalkeeper's Game developed by NeuroMat (game.numec.prp.usp.br). Acting as a goalkeeper, the volunteers were instructed to save as many penalty kicks as they could. The goalkeeper's choices and the kicker's sequence of shots were represented by the symbols 0, 1, and 2, being left, center or right, respectively. A context tree model generated the kicker's sequence of shots. The model generates sequences of kicks where the second event varies, i.e., after each symbol 1, there is a higher probability of symbol 2 (0.7) and a lower
probability of 0 (0.3), for example: 1, 2, 0, 1, 0, 0. This sequence generates the following contexts: 1, 2, 00, 10 and 20. This study aimed to investigate the response times (RT's) and corticospinal excitability (CS) during the Goalkeeper Game. Ten healthy right-handed male volunteers (18–30 years old) were recruited. The index, middle and ring fingers were positioned on the buttons of a keyboard. There were 1200 trials divided in 6 blocks of 200 trials. Motor evoked potentials (MEPs) and RTs were recorded in trials with transcranial magnetic stimulation (TMS) in blocks 2, 4 and 6. The remaining trials were recorded without TMS. TMS pulses were applied 400 ms before the "go" signal. The RT was the time between the go signal and the goalkeeper's choice, after which there was a feedback animation with the trial result. RT's and MEPs of the first dorsal interosseous muscle (FDI) were analyzed. Context trees estimated from RT's and MEPs were retrieved employing the context algorithm. The algorithm associated with Kolmogorov-Smirnov tests if the distribution of data for each context is significantly different (p<0.05). A mode tree was estimated based on the most frequently retrieved contexts with the context tree of each subject. Mode trees could be retrieved using RT's and MEPs, showing the same structure as the kicker's tree. Furthermore, relative MEPs for context 10 (with low probability of occurrence) tended to have larger amplitudes. Preliminary results suggest that recovery of the context tree with MEPs is feasible. Additionally, the MEPs show a tendency to have larger amplitudes after an infrequent context and after a prediction error in this context. These results suggest that the ability to identify statistical regularities can be retrieved through corticospinal excitability, reproducing rules that govern the kicker's tree, and that MEPs tend to be larger after surprising and error contexts.

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2-G-98 - Effect of contextual uncertainty on the expression of motor memories

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<u>Details</u>

Human dexterity relies on forming and managing multiple motor memories. A recent repertoire learning model (COIN) suggests that a participant is in one context at a time and this context determines the sensorimotor mapping (from action to consequences) that is stored in a motor memory. Thus, context tags motor memories and inferring the context dictates which memory is expressed. A key input to contextual inference is sensory cues (e.g., the visual appearance of an object can determine its dynamics). Here we ask how memory selection is affected by uncertainty in contextual inference (driven by noisy cues) and how an explicit decision about context prior to movement affects memory expression.

We conducted experiments where participants made reaching movements in one of two opposing force fields. The direction of a 0.6s random dots motions stimulus (varying in coherence) indicated the direction of the field (context) before the movement, thus manipulating cue reliability across trials. In experiment 1, participants first moved in an initial segment with the field and then followed-through in left or right direction indicating their perceived motion direction. Conversely, in experiment 2, participants performed a lead-in movement (left vs. right) in which they indicated their perception of

dot motion direction before they made the movement through the field. In experiment 1, the motor output was a mixture of the outputs appropriate for each context, with more mixing for lower coherence (greater uncertainty). In contrast, in experiment 2, participants expressed only the memory consistent with their pre-movement choice.

We modeled adaptation under uncertainty using a Bayesian observer that infers context from noisy input. The report (follow-through or lead-in direction) corresponded to motion direction with higher belief. We modeled using two strategies: model averaging (MA: expressing each memory weighted by its inferred belief) and model selection (MS: expressing only the most likely memory). Overall, model fitting supported MA in experiment 1 and MS in experiment 2. We also computed a hybrid model—an interpolation between these extremes—in which samples (n_{samp}) are taken from the full posterior and the decision is based on whether the majority of samples favor left/right. Low/high n_{samp} imply MA/MS, respectively. Estimates of n_{samp} were higher in experiment 2 than in experiment 1 (p<.01), suggesting that, when participants chose the context before movement, they expressed the chosen memory. In contrast, without an explicit choice, the motor output was a weighted mixture of both memories.

Our results parallel perceptual decision-making, where perception can be conditioned based on a binary choice (Jazayeri & Movshon 2007). By revealing how explicit context decision shape motor memory, we link perceptual decision-making to motor execution, offering an integrated view of how the brain handles contextual uncertainty.

2-G-99 - Mechanisms underlying explicit strategy discovery in motor adaptation

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Details

Motor adaptation, the process of correcting motor errors through feedback and practice, keeps our movements well-calibrated in response to changes in the body and environment. While motor adaptation is often viewed as an implicit, non-deliberative process, many studies have shown that explicit strategies are frequently invoked to offset a perturbation. The mechanism by which these strategies are discovered remains unknown. To investigate this, we designed a novel reaching task that isolates explicit strategy discovery. Participants were instructed to counteract a visuomotor perturbation by moving a cursor on the screen and confirming their corrective aim with a click. Decisions were made with minimal time pressure and continuous veridical cursor feedback during the decision phase, reducing the influence of sensorimotor noise and other more implicit learning processes. We recruited a large, online crowdsourced sample of 350 participants (50 per group), each experiencing a distinct perturbation (gain, clockwise/counterclockwise rotation, cardinal/diagonal reflection), allowing us to compare strategy discovery across a representative and wide range of perturbation types. At the group level, we found a clear hierarchy in visuomotor perturbation complexity. Participants adapted fastest to gain perturbations, followed by cardinal mirror reflection, rotation, and slowest to a diagonal mirror reflection. This ranking provides the first empirical measure of which perturbation types are easier or harder to counteract, possibly reflecting their frequency in everyday life. At the individual level, participants varied widely in their learning strategies. Some made abrupt jumps in performance ("moments of insight") while others engaged in systematic exploration ("sign flips") correctly estimating the perturbation's magnitude but oscillating between correct and incorrect directions. These behavioral analyses demonstrate that strategy discovery is not a process of gradual error reduction, where performance incrementally adjusts toward the sensorimotor solution. Instead, strategic performance is

a form of hypothesis testing, where participants evaluate action-outcome hypotheses—such as rotations, reflections, or gain adjustments—and use sensory feedback to determine which spatial transformation best explains the perturbation. Formal computational modeling supports this interpretation: A model that includes hypothesis testing provides a better fit to both individual and group data than that of gradual error reduction. Existing models fail to capture participants' behavior when greater exploration is used to develop a suitable strategy. These findings offer new insights into the mechanisms driving strategy discovery in motor adaptation.

<u>2-G-100 - Initialization and Impedance modulation ensures stability when controlling objects with</u> <u>uncertain dynamics</u>

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<u>Details</u>

Humans can easily perform tasks like spreading a tablecloth or tying shoelaces. However, manipulating such non-rigid objects presents complex dynamical challenges. For instance, when carrying a cup of coffee, the coffee exhibits unpredictable dynamics and generates forces that can lead to instability. Previous research has shown that humans prepare the system's initial conditions and select interaction frequencies to ensure stable dynamics. However, it remains unclear how these strategies adapt when the physical properties of objects, like the mass of a cup, are uncertain or difficult to estimate.

We hypothesize that humans tune their mechanical impedance to manage unpredictable dynamics arising from nonlinearities and uncertainties about object properties. Inspired by our previous work on the task of transporting a cup of coffee, we used a simplified cup-ball system modeled as a cart-pendulum. Participants controlled the cup's position on a screen in one dimension by manipulating the handle of an admittance-controlled robotic manipulandum. They oscillated the cup at their preferred frequency without losing control of the ball. Participants were also encouraged to 'jiggle' the cup prior to starting the rhythmic task to prepare the cup and ball's states.

We measured grip force on the handle as a proxy for the mechanical impedance of the arm. To introduce uncertainty about object properties, we manipulated the pendulum's length. Participants completed two experimental protocols, counterbalanced in order: i) random — the pendulum length changed randomly from trial to trial without explicit cues, and ii) blocked — the pendulum length remained constant across trials. The ball's angle at the end of the preparation phase and the cup's oscillation frequency were used as measures of preparatory and interaction strategies. Stability was defined by the variability of the relative phase between the cup and ball.

Participants took more time to prepare the system in the random condition compared to the blocked condition. In both conditions, they controlled the relative phase to either in-phase (0°) or anti-phase (180°) before starting the rhythmic task. Participants flexibly adjusted both the ball's initial angle and the cup's frequency to stabilize ball dynamics in both conditions. We validated these results through forward simulations of the cup-ball system. We also compared relative phase stability with other optimization criteria, including applied force, smoothness of the applied force, and the risk of losing the ball. Using a grip force sensor, that measured isometric grip force as a proxy for impedance, we showed that participants increased their impedance during preparation, with significantly higher impedance observed in the random condition for both preparation and rhythmic phases. A future goal is to model

the increase in mechanical impedance as a response to system uncertainty, using computational approaches such as stochastic optimal control.

<u>2-G-101 - Embodied human modeling and control: integrating musculoskeletal and motion-related</u> <u>sensory systems</u>

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Details

The human body serves as the primary agent for executing movements, behaviors, and interactions with the physical world. This paper presents a comprehensive, anatomically accurate model of the human musculoskeletal system, encompassing bones, joints, and skeletal muscles, along with vision and other sensory inputs relevant to human motion. The model is dynamically controllable, enabling the simulation of a wide range of movements and interactions. Using high-dimensional stage-wise reinforcement learning, we demonstrate that realistic locomotion, manipulation, and human-machine interaction can be achieved through sensorimotor integration. This work provides deeper insights into human sensorimotor behavior in an embodied context and facilitates more quantitative studies of human-machine-environment interactions.

<u>2-G-102 - Involuntary visuomotor feedback responses reflect partner goals during jointly coordinated</u> <u>movements</u>

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<u>Details</u>

From shaking hands with a colleague to a therapist assisting a patient, we often coordinate our actions with others. Past work has suggested that humans form neural representations of a partner's goal. Yet it is unclear how a representation of a partner's goal might influence rapid feedback responses. Here we tested the idea that the nervous system incorporates knowledge of a partner's goal, which we predicted would be used to tune rapid feedback responses. To investigate, each participant of a human pair grasped the handle of one of two robotic manipulanda. Each screen displayed the participant's own cursor, their partner's cursor, and a jointly controlled cursor at the midpoint between their hands. Participants had vision of both their own target as a solid red rectangle (self target) and their partner's target as a hollow blue rectangle (partner target). We manipulated target width to test whether participants would form a representation of their partner's goals. We used a long rectangular target that was task irrelevant, since participants did not have to correct for lateral deviations to successfully move the jointly controlled cursor into the target. Conversely we used a short rectangular target that was task relevant, since participants had to correct for lateral deviations. We had four experimental conditions: partner-relevant / self-relevant, partner-irrelevant / self-relevant, partner-relevant / self*irrelevant, partner-irrelevant / self-irrelevant.* Participants were instructed to move the center cursor from a start position into their own target. Critically, participant success only depended on the jointly controlled cursor moving into their own target. To probe feedback responses, on a subset of trials each participant's hand was constrained to a force channel when the jointly controlled cursor jumped

laterally and then back to its original position. We measured the lateral force applied to the channel during the involuntary visuomotor feedback response epoch (180-230 ms). Remarkably, we found that participants displayed significantly greater involuntary visuomotor feedback responses in the *partner-relevant / self-irrelevant* condition compared to the *partner-irrelevant / self-irrelevant* condition (p < 0.001). That is, participant involuntary feedback responses were higher when their partner had a relevant target compared to when their partner had an irrelevant target. Our result aligns with the idea that the nervous system forms a representation of a partner to tune involuntary visuomotor feedback responses. We then used a differential game theory, optimal feedback controller to model two interacting humans that had a representation of one another. This controller captured feedback responses for each condition when considering both a self and partner cost function. Collectively, our behavioural results and computational model suggest that the nervous system tunes rapid feedback responses using a representation of a partner's goal.

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