The Dynamics of Motor Control: Circuit Interactions in Health and Disease

Mercè Masana, Ramón Reig, Roberto Leiras,
Ilary Allodi, Julien Bouvier, Graziana Gatto, Lora Sweeney, Maarten Zwart
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PROGRAM

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08:30-09:00 **Registration**

09:00-09:10 **Welcome & Opening remarks,** Mercè Masana, Ramón Reig, Roberto Leiras

09:10 **Session 1: Cortico-striatal Architecture and Circuit Mechanisms for Motor Control**

Chair: Mercè Masana, *University of Barcelona (Spain)*

09:10-09:30 **Harsh Kanodia**, *Biozentrum and FMI (Switzerland)*

"Projection-defined modules reveal mouse motor cortex architecture"

09:30-09:50 **Jorge Maldonado Torres**, *Instituto de Neurociencias CSIC-UMH (Spain)*

"Divergent Synaptic Fingerprints of Frontal and Somatomotor Inputs in the Dorsolateral Striatum"

09:50-10:10 **Daniel Ramandi**, *Djavad Mowafaghian Centre for Brain Health (Canada)*

"Cortical and striatal circuit recruitment during a voluntary motor task in a mouse model of Huntington's disease."

10:10-11:30 **Poster Session I (Posters 1-20) and coffee break**

11:30 **Session 2: Population Dynamics Encoding Movements**

Chair: Ramón Reig, *Instituto de Neurociencias CSIC-UMH (Spain)*

11:30-11:50 **Charlotte Bichara**, *Institute Cellular and Integrative Neurosciences (France)*

"Phase-dependent and anticipatory cortical control of hindlimb locomotion"

11:50-12:10 **Phillip Bokiniec**, *Queensland Brain Institute (Australia)*

"Population coding of locomotion by sensory afferent neurons in the awake mouse"

12:10-12:30 **Omar Refy**, *University of Copenhagen (Denmark)*

"Neuraxis-wide population dynamics during voluntary wrist movement in macaque"

12:30-14:00 **Lunch break**

14:00 **Session 3: Descending Pathways for Action Initiation and Execution**

Chair: Roberto Leiras, *University of Copenhagen (Denmark)*

14:00-14:20 **Rémi Ronzano**, *University College London (United Kingdom)*

"Spinal circuits encode a map of the trunk to control skin twitches"

14:20-14:40 **Giacomo Sitzia**, *University of Copenhagen (Denmark)*
"A Subthalamic–Brainstem Circuit for Locomotor Initiation"

14:40-15:00 **Vanessa Stempel**, *Max Planck Institute for Brain Research (Germany)*
"Midbrain Circuits for Defensive Behavior Execution"

15:00-15:05 **Group Photo**

15:05-16:30 **Poster Session II (Posters 21-40) and coffee break**

16:30 **Session 4: Spinal Circuits Connectivity in health and disease**
Chair: Lora Sweeney, *Institute of science and technology Austria (Austria)*

16:30-16:50 **Sandrina Campos Maçãs**, *University Hospital of Cologne (Germany)*
*"*Mapping the connectivity of spinal cord projection neurons"

16:50-17:10 **Beck Strohmer**, *University of Copenhagen (Denmark)*
"Closed-loop proprioceptive feedback in a spinal circuit model of ALS"

17:10-17:30 **Patricia del Cerro de Pablo**, *Paris-Saclay Institute of Neuroscience (France)*
"Plasticity of medullary descending pathways after spinal cord injury and trans-spinal magnetic stimulation"

17:30-17:45 **Conclusion and Final remarks**

17:45-20:00 **Free time to rest, stretch and network until dinner**

20:00-22:30 **Dinner at Restaurant "SAONA Aribau" (only for registered attendees)**
Calle Aribau 131, 08036, Barcelona.
https://www.gruposaona.com/restaurante/saona-aribau/

Talk 1: Projection-defined modules reveal mouse motor cortex architecture

Harsh Kanodia*[1,2], Antonio Falasconi*[1,2], Nicholas Lusk[3], Shenqin Yao[3], Rui M. Costa[3], Hongkui Zeng[3], Silvia Arber[1,2]

[1] Biozentrum, University of Basel, Basel, Switzerland
[2] Friedrich Miescher Institute for Biomedical Research, Basel, Switzerland
[3] Allen Institute for Brain Science, Seattle, WA, United States

The motor cortex (MO) coordinates movement through its complex connectivity. However, despite evidence for functionally and anatomically distinct areas, organizing principles of MO lack consensus. Here we show that the subcortical projections of mouse MO define 16 different modules. Subcortical output divergence aligns to variation in modular cortico-cortical connectivity and cell-type composition, delineating two spatial MO axes. Along one axis, primary MO couples reciprocally to somatosensory cortex and secondary MO to frontal areas, with differential excitatory neuron compositions specifying the two regions. Along the orthogonal axis, somatosensory cortex inputs stratify modules, together with non-sensorimotor cortical wiring and aligned cell-type signatures. The cortical two-axes logic extends to subcortical targets, with striatum, thalamus and brainstem following distinct convergence-divergence rules, differentially integrating cortical inputs. Together, this work reveals a logic by which the anatomical architecture of the mouse MO integrates into brainwide and specific neuronal networks.

Talk 2: Divergent Synaptic Fingerprints of Frontal and Somatomotor Inputs in the Dorsolateral Striatum

Jorge Maldonado-Torres[1], María Sáez[1], Josepa Rico-Salvador[1], Ramón Reig[1]

[1] Instituto de Neurociencias CSIC-UMH, Alicante, Spain

The basal ganglia are a group of highly interconnected subcortical nuclei, with the striatum serving as the main entrance structure, integrating activity from both the cortex and the thalamus. Motor and somatosensory cortical areas, together with the prefrontal association area (FrA), send dense projections to the lateral region of the dorsal striatum (DLS), a structure involved in the control of learned movements. These cortical inputs target single striatal GABAergic projection neurons, called Medium Spiny Neurons (MSNs), as well as several classes of interneurons, including parvalbumin and somatostatin-expressing interneurons. In this work, we aim to understand how sensorimotor and prefrontal cortical areas modulate MSN activity, as well as their impact on movement. Therefore, we investigate the synaptic dynamics of M1, S1, and FrA inputs onto MSNs involved in orofacial movements. We performed patch-clamp recordings from DLS-MSNs in anesthetized and awake head-fixed mice, while optogenetically stimulating glutamatergic cortical neurons from these three areas, simultaneously acquiring high-speed video of orofacial behavior.

Our preliminary results in anesthetized and awake head-fixed animals show that FrA and M1 exert stronger synaptic inputs onto MSNs compared with S1, producing larger and more sustained depolarizations following optogenetic stimulation. However, short-term synaptic dynamics, pair-pulse ratio and short-term depression, differ across cortical areas, with S1 producing the strongest levels of depression. In addition, we analyzed the mice movements during cortical activation to assess how synaptic transmission influences orofacial activity and, conversely, how ongoing behavior impact on synaptic dynamics.

Talk 3: Cortical and striatal circuit recruitment during a voluntary motor task in a mouse model of Huntington's disease

Daniel Ramandi[1], Marja Sepers[1], Euyoung Park[1], Timothy H. Murphy[1], Lynn A. Raymond[1]

[1] Djavad Mowafaghian Centre for Brain Health, University of British Columbia, Vancouver, Canada

Voluntary movement requires coordinated corticostriatal signaling and is impaired in Huntington's disease (HD). We studied 6-8-month-old zQ175 mice and WT littermates (6 WT, 5 zQ175) in a lever-pull task in automated home-cage and head-fixed settings. Thy1-jRGECO1a mice (red Ca^{2+} indicator; excitatory neuron–selective) were imaged transcranially through intact-skull cranial windows, and received dorsal striatum (DS) AAV1-iGluSnFR (green glutamate sensor) plus an angled optical fiber for photometry, enabling simultaneous cortical Ca^{2+} imaging and DS iGluSnFR transients. In home-cage, zQ175 had lower success and more overshoot failures (impaired movement refinement/feedback control). Under head fixation, engagement and success were similar. Cortical activity showed robust primary motor activation after pull onset in both genotypes, but reduced secondary motor (M2) recruitment in zQ175. DS iGluSnFR signals were pull-locked with similar peak amplitude/latency, but slower decay in zQ175, consistent with sustained excitatory drive and/or slowed clearance. Whole-cell current-clamp in M2 pyramidal neurons found no differences in resting potential, rheobase, or frequency-current (F-I) curves, arguing against altered intrinsic excitability. Overall, results support circuit-level corticostriatal incoordination in zQ175. Ongoing work will test whether disrupted M2 connectivity drives these dynamics and whether targeted M2 activation rescues circuit signatures and performance.

Talk 4: Phase-dependent and anticipatory cortical control of hindlimb locomotion

Charlotte Bichara[1], Gilles Delbecq[2], Léa Favier[1], Philippe Isope[1], Antoine Valera[1], Matilde Cordero-Erausquin[1]

[1] Institute of Cellular and Integrative Neurosciences, Strasbourg, France
[2] Institute of Neuroscience of la Timone, Marseille, France

Descending cortical control of locomotion orchestrates coordination between cortical and spinal circuits during complex movements. While motor cortex activity is known to modulate locomotion, the temporal dynamics and functional significance of this control during natural, adaptive locomotion remain poorly understood.

Using in vivo electrophysiological recordings combined with unbiased 3D kinematic tracking in freely moving mice, we characterized cortical activity during locomotor tasks of increasing complexity. We identified two distinct modes of sensorimotor cortical involvement. Beyond the expected phase-locked activity tracking locomotor rhythm, we discovered a preparatory mode characterized by transient activity precisely aligned with locomotor phase transitions and preceding key mechanical events by ~200 ms. This temporal lead is incompatible with direct motor commands and instead reflects an anticipatory signal directed toward spinal circuits. Critically, neurons displaying preparatory activity increased with task difficulty, and became increasingly focused on anticipating paw contact with ladder rungs rather than flat surfaces. Optotagging experiments confirmed that corticospinal neurons constitute a primary substrate of this preparatory activity.

These findings reveal that cortical control of locomotion operates partly through feedforward gating of spinal processing. This preparatory mechanism scales with task demands and enables adaptive locomotor control in challenging environments, fundamentally revising our understanding of cortical contributions to movement coordination.

Talk 5: Population coding of locomotion by sensory afferent neurons in the awake mouse

Phillip Bokiniec[1], Ryan J. Gibbons[1], Clarissa J. Whitmire[1,2]

[1] The University of Queensland, Queensland Brain Institute, St Lucia, Brisbane, Queensland, Australia
[2] The University of Queensland, School of Electrical Engineering and Computer Science, St Lucia, Brisbane, Queensland, Australia

Mammalian locomotion arises from the coordinated interaction between motor commands generated by spinal interneurons, and sensory feedback originating from the periphery. Peripheral sensory neurons continuously signal joint position, limb movement, and mechanical deformation of the skin, providing a rich representation of locomotion. However, how large populations of sensory neurons encode and contribute to distinct locomotor phases remains unclear. Here, we addressed this by performing in vivo two-photon calcium imaging of the fourth lumbar dorsal root ganglion in awake, locomoting, spine-fixed mice. To image diverse populations of sensory neurons, we used systemic viral delivery in postnatal day 5 pups to drive broad GCaMP7s expression. Adult mice underwent surgical implantation of a spinal post for fixation, and a glass coverslip over the dorsal root ganglion to provide chronic optical access to sensory neurons. Following habituation to spine-fixed locomotion on a running wheel, neural activity was measured during self-generated movement while hindlimb position was recorded using multiple behavioral imaging cameras. Population recordings across peripheral sensory neurons, whilst mice either walked or ran on a running wheel, revealed coordinated activity in response to self-generated behavioral events. Sensory neuron activity showed bidirectional response properties with both increased and decreased fluorescence across movement bouts. Presumed tactile events whereby the mouse was not locomoting but instead pressing the hindpaw into the surface of the running wheel, also led to salient neural responses across the population. Our results reveal that peripheral sensory afferent populations provide a mixed representation of movement and tactile information during self-generated locomotion.

Talk 6: Neuraxis-wide population dynamics during voluntary wrist movement in macaque

Omar Refy[1], Eberhard Fetz[2], Jens Bo Nielsen[1]

[1] University of Copenhagen, Copenhagen, Denmark
[2] University of Washington, Seattle, WA, United States

Goal-directed movement arises from coordinated neural activity spanning the motor cortex, spinal cord, and peripheral sensory pathways, yet how population dynamics are organized across these hierarchical levels remains incompletely understood. Here, we characterize neuraxis-wide population dynamics during single-joint wrist isometric flexion-extension tasks in five macaque monkeys. Neural recordings were obtained using single tungsten microelectrodes from primary motor cortex (M1; n = 1), cervical spinal interneurons (n = 2), and dorsal root ganglia (DRG; n = 2), simultaneously with intramuscular electromyography (EMG) from up to twelve forearm muscles and joint torque measurements.
Across all recording sites, neural activity exhibited prominent oscillatory structure systematically related to movement phase. However, the geometry and dimensionality of these dynamics differed across levels of the motor axis. In M1, both interneuronal populations and identified corticomotoneuronal (CM) cells displayed robust rotational dynamics, evident as clear two-dimensional trajectories in principal component space. In contrast, spinal interneuronal populations exhibited predominantly one-dimensional, alternation-like dynamics closely resembling the temporal structure of muscle activity and joint torque. DRG populations displayed intermediate dynamics, reflecting their position at the interface between descending motor commands and peripheral sensory feedback.
Together, these findings reveal heterogeneous yet structured population dynamics across the motor axis. These findings indicate a heterogenous structure of motor circuitry activity during voluntary movement where cortical, spinal, and sensory populations appear to operate with distinct dynamics that must be precisely coordinated to generate coherent, stable, and controlled movement.

Talk 7: Spinal circuits encode a map of the trunk to control skin twitches

Rémi Ronzano[1], Ka Yee Chan[1], Manon Papadiamandis[1], Ugo Momi[1], Marco Beato[2], Robert M. Brownstone[1]

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Reflexive skin twitches are stereotypical behaviours, triggered in most mammals by mechanosensory stimuli. The neural circuits controlling this behaviour are thought to lie in the spinal cord, with motor neurons positioned in the lower cervical spinal cord innervating the cutaneous maximus muscle responsible for the twitches. The spatial matching of the motor output to the location of the sensory stimulus points to selective innervation of particular cutaneous maximus motor neurons by specific sensory-responsive circuits organised in a spatially-dependent manner involving propriospinal projections. Using mouse genetics and viral tracing, we show that a subset of dorso-lateral dI3 neurons distributed along the thoracic and rostral lumbar segments forms ascending projections to motor neurons mediating skin twitches. These dI3 neurons receive direct mechanosensory afferents and their projections are somatotopically organized to map a two dimensional space onto specific sub-compartments of the cutaneous maximus motor pool. Furthermore, direct in vivo optogenetic stimulation of dI3 ascending projections in the cervical spinal cord induces skin twitches. Together, we demonstrate the circuit basis of a spinal sensory-motor representation of the dorsolateral trunk that participates in an ethological behaviour shared by most mammals allowing them to reduce the burdens of irritants such as insects.

Talk 8: A Subthalamic–Brainstem Circuit for Locomotor Initiation

Giacomo Sitzia[1], Simona A. M. Bucolo[1], Luisa Abels[1], Ole Kiehn[1]

[1] Department of Neuroscience, University of Copenhagen, Denmark

Locomotion is a fundamental motor behavior that can be initiated volitionally or driven by sensory stimuli, depending on context. Brainstem and spinal cord circuits are ultimately responsible for locomotor command generation and execution; however, how these circuits are engaged by upstream inputs remains unclear. Glutamatergic neurons of the caudal pedunculopontine nucleus (Vglut2-cPPN) are essential for the initiation and speed control of exploratory locomotion. Anatomical studies show that Vglut2-cPPN neurons receive monosynaptic input from basal ganglia output regions, including the subthalamic nucleus (STN) and substantia nigra pars reticulata. Here, we functionally investigated these pathways, focusing on the STN–cPPN projection. Selective optogenetic activation of STN-cPPN neurons elicited forward, symmetric locomotion, whereas optogenetic inhibition disrupted self-paced locomotion. Using viral strategies, we are linking STN-cPPN projections to downstream targets in the medulla. Combining retrograde viral tracing with in situ hybridization, we found that STN-cPPN neurons are a unique STN cell type. The STN is a major target for deep brain stimulation in Parkinson's disease (PD). We therefore tested whether activation of the STN–cPPN pathway could promote locomotion in a mouse model of acute parkinsonism induced by dopamine receptor antagonism. Activation of STN-cPPN neurons reversed akinesia and reliably promoted locomotion in haloperidol-treated mice. Together, these findings refine current models of basal ganglia organization for locomotor control, placing the STN–PPN pathway as a central node linking basal ganglia output to spinal locomotor circuits. We propose that targeting the STN–PPN pathway may represent a therapeutic strategy for alleviating locomotor deficits in PD.

Talk 9: Midbrain Circuits for Defensive Behavior Execution

Vanessa Stempel[1], Alicia Strosche[1], Ayu Tamaki[1], Jonathan Mader[1], Eloah Biasi[1], Petros Chalas[1]

[1] Max Planck Institute for Brain Research, Frankfurt, Germany

Instinctive behaviors – such as escape from threat, or hunting of prey – are critical for an animal's survival and are highly conserved across the animal kingdom. In vertebrates, the midbrain plays a central role in translating sensory information into an appropriate motor response, with several interconnected structures controlling the initiation and execution of instinctive behaviors. The midbrain cuneiform nucleus (CnF) has classically been associated with the control of high-speed locomotion but whether the CnF contributes to locomotion as a general motor output, or selectively to locomotion in particular behavioral contexts, remains unclear. Using neural activity recordings in freely moving mice, we compared the activity of CnF neurons during locomotion in different behavioural 'contexts'– including exploration, hunting and escape – and found that CnF neurons are preferentially recruited during defensive locomotion, in comparison to locomotor bouts during exploration or hunting. Supporting this, optogenetic stimulation of glutamatergic CnF neurons reliably elicited shelter-directed escapes. Furthermore, CnF activity reflected the perceived threat independent of the behavioral outcome, suggesting a role in threat representation. Together, our findings establish the CnF as an important brain region in the midbrain defense circuit, suggesting a role as sensory-motor integrator to gate defensive behavior output.

Talk 10: Mapping the connectivity of spinal cord projection neurons

Sandrina Campos Maçãs[1], Quinn Silverman[1], Graziana Gatto[1]

[1] University Hospital of Cologne, Department of Neurology, Cologne, Germany

Execution and adaptation of motor behaviors rely on the dynamic interactions of networks of neurons across the peripheral and central nervous system. Spinal circuits, functioning as the final checkpoint for motor execution and the second relay in sensory perception, are a critical hub for sensorimotor integration. Spinal circuits, primarily made of interneurons, also include various classes of projection neurons that convey somatosensory information to the brain. Yet, how these projection neurons are embedded within the spinal circuits, their molecular identities, and supraspinal targets remain unclear.

Using viral and intersectional genetic strategies to label all spinal ascending tracts, we assessed 1) the brain regions innervated by spinal ascending projections, 2) the postnatal refinement of the axonal projections, 3) the brain region-specificity of subtypes of spinal projection neurons, and 4) the spinal distribution of brain area-specific projection neurons. Analysis of the complete projectome demonstrates that ascending spinal projections display a certain degree of topographic organization and structurally consolidated during postnatal development. We confirm known targets (cerebellum, lPBN, VPL), and novel anatomical evidence of spinal projections to the dorsal raphe. Within the DCN, direct projections from dorsal root ganglia neurons principally contribute to the external cuneate innervation, while spinal projections target the cuneate and gracile nuclei. The relative density and distribution of spinal projections are subtype-specific. The dorsal horn populations target widespread sensory and motor-related areas, whereas ventral horn populations target specific motor-related areas exclusively. In parallel and using retroviral approach, we observed spinal-PoT projection neurons are mostly contralateral and reside at cervical and lumbar levels, whereas spinal-lPBN projection neurons are ipsilateral and contralateral and distributed across all spinal levels.

The detailed map of the spinal ascending connectome that is emerging from our analyses is starting to clarify how ongoing actions and detected somatosensory and proprioceptive cues are relayed to supraspinal regions for long-term adaptation and re-planning of behavior.

Talk 11: Closed-loop proprioceptive feedback in a spinal circuit model of ALS

Beck Strohmer[1], Shravan Tata Ramalingasetty[2], Jessica Ausborn[2], Simon M. Danner[2], Ilary Allodi[3]

[1] University of Copenhagen, Copenhagen, Denmark
[2] Drexel University, Philadelphia, United States
[3] University of St Andrews, St Andrews, United Kingdom

Spinal-onset amyotrophic lateral sclerosis (ALS) is marked by early disruption of inhibitory V1 interneuron synapses within locomotor central pattern generators (CPGs), the spinal circuits responsible for generating rhythmic movement. This initial loss of V1 synaptic input is followed by dysregulation of inhibitory V1 interneurons, subsequent dysfunction of excitatory V2a interneurons, and ultimately motoneuron degeneration. Experimental stabilization of V1 synapses restores locomotor function by preserving both V1 inhibitory interneurons and motoneurons, and recent work from our lab indicates that such interventions may also protect excitatory V2a interneurons, pointing to circuit-level mechanisms that extend beyond motoneuron loss. However, the contribution of degenerating sensorimotor feedback pathways linking muscles, interneurons, and motoneurons to overall circuit failure and their influence on therapeutic efficacy remains unclear.

Here, we develop a computational model of a locomotor CPG incorporating proprioceptive feedback derived from muscle models with Hill-type dynamics. The biophysical component is represented by a pendulum model of a simplified single hindlimb joint, driven by antagonistic muscles that generate flexion and extension. These muscle models provide proprioceptive input that modulates the stretch reflex, a feedback pathway known to deteriorate during ALS. The model incorporates stage-dependent degeneration of this feedback pathway alongside progressive neuronal and synaptic loss, enabling a novel, integrative framework for examining how sensorimotor feedback failure contributes to circuit breakdown in ALS. By modelling progressive feedback degeneration between a biophysical model and a biologically-plausible neural circuit, this work introduces a new approach to studying disease progression at the circuit level. The findings aim to generate testable predictions regarding the interplay between sensorimotor feedback deficits, network degeneration, and potential intervention strategies.

Talk 12: Plasticity of medullary descending pathways after spinal cord injury and trans-spinal magnetic stimulation

Patricia del Cerro de Pablo[1], Laurine Moncomble[2], Auregan Lamour[1], Nicolas Guérout[2], Julien Bouvier[1]

[1] University Paris-Saclay, CNRS, Paris-Saclay Institute of Neuroscience, France
[2] Saints-Pères Paris Institute for Neurosciences, University of Paris Cité, France

Various neuronal populations in the brainstem, particularly the medulla, are crucial for controlling distinct aspects of movement, including posture and locomotion. Despite the known potential plasticity of descending medullary pathways after spinal cord injury (SCI), the exact nature, functional implications, and modulation of such plasticity by therapeutic approaches remain unclear. We explore here, in a mouse SCI model of thoracic hemisection, the comparative plasticity of specific subtypes of descending medullary neurons and the impact of a non-invasive therapy, repetitive trans-spinal magnetic stimulation (rTSMS).

Expectedly, retrograde tracing revealed a marked reduction in the number of ipsilateral labeled medullary neurons following thoracic hemisection, while the contralateral ones were largely preserved. However, subtype-specific analyses demonstrated distinct responses to injury among medullary populations, notably with respect to their innervation of the ipsilateral and contralateral spinal cord. Importantly, a 14-day rTSMS treatment improved recovery, both anatomically and functionally. Indeed, we observed changes in the organization and distribution of specific medullary projections in the spinal cord, suggesting the modulation of plasticity in selective pathways. Functionally, rTSMS significantly improved the recovery of skilled, adaptive locomotion.

These findings refine our understanding of plasticity in descending medullary pathways after SCI, and identify this plasticity as one potential underpinning of the rehabilitative effects of neuromodulatory therapies.

Poster List

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Poster 2: Ninon Peysson (France) - *All-optical mapping of the mesencephalic locomotor region in the larval zebrafish*

Poster 3: Austin Chuang (USA) - *A Neuromechanical Model Reveals that dI3-to-γ Pathways Provide Spindle Feedback Control of Gait Kinematics and Phase Transitions*

Poster 4: Laura Bushelli (USA) - *Afferent feedback enables robust sit-to-stand transitions in response to V3 stimulation: a neuromechanical modeling study*

Poster 5: Simrandeep Kaur Sidhu (Denmark) - *Restoration of Locomotor Function in a Chronic Parkinsonian Mouse Model by Selective Activation of Brainstem Command Neurons*

Poster 6: Jacinthlyn Sylvia Suresh (Canada) - *Modulation of locomotion and orienting movements by D2 receptor-expressing neurons in the gigantocellular reticular nucleus*

Poster 7: Xinyu Jia (France) - *All-optical dissection of a spatially organized reticulospinal circuit for locomotor initiation and maintenance*

Poster 8: Ines Klein (Germany) - *Spinal circuits for locomotor adaptation*

Poster 9: Axel E. Gorostiza (Germany) - *Symmetry break and leg specific roles during curve walking in Drosophila*

Poster 10: Marie Yahia (France) - *A serotonergic sensory-gating pathway for adaptive locomotion*

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Poster 12: Manuela Rizzi (UK) - *Spatial transcriptomics reveals distinct molecular signature of motor neurons and interneurons in control and pre-symptomatic stages of an ALS mouse model*

Poster 13: Katherina Rees (USA) - *Corticospinal Connectivity after Developmental Damage: Circuit Plasticity & Functional Outcomes*

Poster 14: Mahan Hosseini (Germany) - *AutoGaitA: A versatile quantitative framework for kinematic analyses across species, perturbations and behaviours*

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Poster 16: Maryam Givehchi (Spain) - *Disrupted cAMP dynamics in the secondary motor cortex during sensorimotor and motor learning behaviour in the R6/1 mouse model of Huntington's disease*

Poster 17: Samuel Fedde (USA) - *Cortico-brainstem pathway compensates for loss of corticospinal output after stroke and spinal cord injury*

Poster 18: Dominic Falardeau (Canada) - *Exploring the role of the premotor trigeminal complex in masticatory function*

Poster 19: Prathigna Thambi Jaishankar (France) - *Gene expression mapping of the mesencephalic locomotor region, reticular formation and spinal motor circuits in larval zebrafish*

Poster 20: Valentina Bova (Spain) - *Contribution of striatal D1-expressing neurons to motor deficits in early and later stages of the Huntington's disease*

Poster 21: Angus Gray (UK) - *Modelling the Emergence of Asymmetric Motor Deficits in Amyotrophic Lateral Sclerosis Using a Bilateral Spinal Central Pattern Generator*

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Poster 27: Evgeny Bondarenko (USA) - *Non-volitional slow breathing training produces persistent reductions in anxiety and stress reactivity via the preBötzinger complex*

Poster 28: Anna Stuckert (UK) - *Investigating the Early Frontotemporal Dementia Phenotypes in a Mouse Model of TDP-43 Proteinopathy*

Poster 29: Haohao Wu (Switzerland) - *Encoding fine-grained forelimb movements through molecularly heterogeneous brainstem neurons*

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Poster 31: Mahalakshmi Dhanasekar (France) - *Cerebrospinal Fluid Noradrenergic Signaling Sustains Motor Arrest through Disruption of Motor Commands*

Poster 32: Laurine Moncomble (France) - *Neuronal activation mapping in the spinal cord following high-intensity trans-spinal magnetic stimulation in mice*

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Poster 34: Manjusha Goli (Canada) - *Fight, Flight, and Firing: Investigating the Effects of Aversive Stimuli on Glutamatergic Cell Activity in the Medial Zona Incerta*

Poster 35: Andrea Giorgi (France) - *Modular V2a reticulospinal circuits orchestrate distinct kinematic strategies for turning*

Poster 36: Pauline Neveu (France) - *Low-intensity magnetic stimulation exerts pattern-dependent effects on tissue repair after spinal cord injury*

Poster 37: Bella Xu Ying (UK) - *Neurons exhibiting anti-motor activity in the Xenopus laevis tadpole hindbrain*

Poster 38: Cameron Burton (UK) - *Coordination of feeding and locomotion behaviors in larval Drosophila: a functional connectomic analysis*

Poster 39: Maarten Zwart (UK) - *The inferior olive transforms upstream sensorimotor errors into cerebellar teaching signals*

Poster 40: Nicolas Guerout (France) - *Repetitive trans-spinal magnetic stimulation promotes repair in inflammatory spinal cord injury through sex-dependent immune modulation*

Poster 1: Uncovering principles in brainstem processing of spatial and directional cues from sensors across the body to motor commands

Elias T Lunsford[1], Claire Wyart[1]

[1] Paris Brain Institute, Paris, France

Animals navigate by transforming distributed sensory inputs into discrete motor actions, yet how stimulus features such as intensity, frequency, and duration are integrated with spatial information to bias action selection remains poorly understood. A major challenge in vertebrate species has been finding emerging principles of how graded sensory signals are converted into categorical motor commands in the brainstem. The lateral line (LL) system of zebrafish constitutes an ideal model to investigate principles in the brainstem underlying the integration of sensory inputs across the body. With responses to directionality across virtually all LL sensors along the larval zebrafish, we uncovered that processing occurs via a simple egocentric framework, in which spatial and directional flow cues converge onto functionally distinct motor command pathways. Building on this foundation, we now ask how variation in stimulus strength and temporal structure shapes the recruitment of sensory interneurons and downstream motor command circuits to determine behavioral output. The LL links peripheral sensors to reticulospinal neurons through only a few synapses, offering a unique opportunity to follow the transformation from stimulus to action at cellular resolution. By systematically varying stimulus direction, intensity, frequency, and duration at each sensor position, we determine how key parameters are encoded within the brainstem to bias the selection of forward locomotion, avoidance turns, and approach behaviors. By systematically varying both the sensor position and temporal or intensity structure of sensory inputs, this work reveals how vertebrate sensorimotor circuits route multidimensional signals along distinct motor command pathways that bias action selection.

Poster 2: All-optical mapping of the mesencephalic locomotor region in the larval zebrafish

Ninon Peysson[1], Kevin Fidelin[1], Claire Wyart[1]

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In vertebrates, stimulation of the mesencephalic locomotor region (MLR) can reliably elicit forward locomotion and represents a promising avenue to recover motor deficits in Parkinson's disease. Yet, MLR neurons are genetically diverse, spatially intermingled, and project widely throughout the brain. Consequently, the effects of MLR stimulation largely vary according to the location and cell type targeted. Linking the soma location of individual MLR neurons with their neurotransmitter phenotype and projection profile is essential at the population level to resolve their contribution and perform efficient stimulations for motor recovery. Here, we leverage the small size and transparency of the larval zebrafish whose MLR contains ~ 200 neurons to unravel their molecular and functional diversity. We first reconstruct in 3D the spatial organization of MLR subpopulations by imaging transgenic lines labeling neurons expressing distinct neurotransmitters or transcription factors. Using photoactivable GFP, we then perform optical retrograde labeling of descending MLR neurons based on their projections in the medulla and spinal cord to link neurotransmitter phenotypes with structural organization. Finally, we implement columnar optogenetic stimulations with digital holography to selectively activate genetically and spatially defined MLR subtypes. We combine this approach with high-speed recordings of tail movements to probe the contribution of MLR neurons to movement initiation, steering modulation or motor arrest. Altogether, our anatomical and functional mapping approaches will clarify the spatial and functional organization of the MLR in a small model organism and should help refining deep brain stimulation strategies.

Poster 3: A Neuromechanical Model Reveals that dI3-to-γ Pathways Provide Spindle Feedback Control of Gait Kinematics and Phase Transitions

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dI3 neurons are glutamatergic premotor neurons located in the deep dorsal horn that integrate sensory information and contribute to locomotor control. In mice, dI3 neuron silencing alters limb kinematics and delays the stance-to-swing phase transition. dI3 neurons exhibit substantial synaptic connections to γ-motoneurons, which control Ia and II spindle sensitivity, positioning dI3s to modulate movement via phase-dependent γ drive. We therefore hypothesize that the effects of dI3 silencing on kinematics and phase transitions arise from γ-mediated control of spindle sensitivity. Because this pathway may also contribute to recovery after spinal cord injury, defining dI3 function has clear translational relevance. To test this hypothesis, we incorporated γ-motoneurons with partial dI3 control to our 2D neuromechanical hindlimb mouse model that couples a spinal locomotor circuitry model to a musculoskeletal model (seven muscles per limb; hip, knee, and ankle joints) via motoneuron output and Ia, Ib, II and cutaneous afferent feedback. γ-motoneurons were modeled to follow α-motoneuron activity. The model was optimized for functional locomotion and closely reproduced kinematics of intact animals. Removing phase-dependent γ activation of ankle extensors resulted in increased dorsiflexion yield after ground acceptance, while reducing hip flexor II spindle sensitivity delayed the stance-to-swing transition and caused hip hyperextension at the end of stance. When combined, these changes mirrored locomotor deficits observed after dI3 silencing. Thus, our modeling results suggest that dI3-to-γ-motoneuron pathways shape spindle feedback, and their disruption can account for kinematic and timing deficits seen after dI3 silencing, underscoring their critical role in adaptive locomotor transitions.

Poster 4: Afferent feedback enables robust sit-to-stand transitions in response to V3 stimulation: a neuromechanical modeling study

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Optogenetic stimulation of lumbar V3 neurons in mice broadly activates hindlimb muscles, eliciting flexor and extensor co-activation, with a bias towards extensor activation. The mouse extends its hindlimbs and transitions smoothly from sitting to standing. Yet, how simple activation of a class of interneurons can induce a controlled transition to stable standing is unknown.

Here, we present a neuromechanical model of a mouse hindlimb including hip, knee, ankle, and metatarsal-phalange joints. Hill-type muscles represent several major flexors, extensors, and bifunctional muscle groups. Proprioceptive feedback signals were connected to a simplified neural network model, implementing low-level spinal reflex circuits. V3 interneurons were modeled to provide excitatory input to interneurons and motoneurons.

Our simulations demonstrated bistable limb dynamics induced by direct V3-driven extensor motoneuron activation, depending on the gradual increase and decrease of V3 neuron activity. As the limb extends, moment arms of knee extensor muscles improve; once sufficient muscle force is produced to overcome gravity a positive feedback loop is triggered: the resulting extension enhances muscle leverage, further increasing torque production and thus driving a rapid transition from flexion to full extension. Incorporating sensory feedback pathways, including Ia reciprocal inhibition, group II excitation, and Ib disynaptic excitation, alongside flexor-extensor coactivation, reduced the bistable range and enabled a smooth, stable control of limb extension in response to V3 stimulation.

These findings suggest that low-level reflex circuits contribute to stabilizing posture and controlling limb responses triggered by broad neural activation, offering insight into mechanisms by which V3 stimulation could induce standing.

Poster 5: Restoration of Locomotor Function in a Chronic Parkinsonian Mouse Model by Selective Activation of Brainstem Command Neurons

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Locomotor control is organized hierarchically, with brainstem structures operating downstream of the basal ganglia to modulate locomotion. The mesencephalic locomotor region (MLR), comprising the pedunculopontine nucleus and cuneiform nucleus, governs locomotion initiation and speed modulation, whereas the pontine nucleus oralis (PnO) controls locomotor steering. In Parkinson's disease (PD), degeneration of nigrostriatal dopaminergic neurons causes basal ganglia dysfunction, disrupting downstream motor control and resulting in locomotor impairments such as bradykinesia, freezing of gait, and turning deficits. Given the hierarchical organization of locomotor control, MLR and PnO dysfunction may contribute to parkinsonian motor deficits. We therefore hypothesized that targeted activation of these nuclei may alleviate motor impairments in chronic PD. To investigate this possibility, we used the MitoPark mouse model. Compared to acute pharmacological and toxin-based PD models, MitoPark mice more closely recapitulate human PD pathology through a progressive, adult-onset phenotype that advances to chronic stages. MitoPark mice display reduced locomotion and turning frequency, and progressively fail to attain higher speeds ranges (10–20 cm/s and >20 cm/s). Using excitatory DREADDs, we show that bilateral activation of glutamatergic MLR neurons improves locomotor function by restoring the speed profile, reducing time spent at low speeds (2–5 cm/s) and increasing occupancy of higher speed ranges, without improving turning behavior. In contrast, combined bilateral activation of the MLR and PnO restored the speed profile and increased the turning frequency, indicating that MLR activation enhances forward locomotion, whereas PnO activation improves locomotor steering. Together, these findings outline promising brainstem targets for improving locomotor function in PD.

Poster 6: Modulation of locomotion and orienting movements by D2 receptor-expressing neurons in the gigantocellular reticular nucleus

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The reticular formation plays a key role in motor control, containing the command systems for initiating, stopping, and directing locomotion. These commands are transmitted to spinal circuits via reticulospinal neurons. In lampreys, reticular regions are targeted by descending dopaminergic pathways (Ryczko et al. 2020 J Neurosci). However, in mammals, the reticular neurons targeted by dopamine and their behavioral roles are unknown. Here we investigated in mice the behavioral role of neurons expressing dopaminergic D2 receptors in the gigantocellular reticular nucleus (Gi), a region involved in the control of stops and orienting movements. Using RNAscope, we identified cells expressing the D2 receptor in the Gi. To activate these Gi D2-positive neurons in vivo, we unilaterally injected a virus in the Gi of D2-Cre mice, enabling Cre-dependent expression of channelrhodopsin. An optical fiber was implanted above the injection site and video recordings were done in an open-field to track body movements. Unilateral photostimulation of Gi D2-expressing neurons reduced locomotor speed and evoked ipsilateral head movements. Using high resolution axial body tracking in a linear corridor, we found that stimulation evoked body orienting movements towards the stimulated side. Altogether, our findings indicate that activation of D2-positive neurons in the Gi decreases locomotor speed and induces ipsilateral body and head orienting movements.

Poster 7: All-optical dissection of a spatially organized reticulospinal circuit for locomotor initiation and maintenance

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Locomotion requires precise coordination of descending motor commands conveyed by reticulospinal neurons (RSNs). How these commands are transformed within the brainstem into executable spinal instructions remains unclear. Here, we address this question in transparent, genetically accessible larval zebrafish by optically recording and manipulating a major RSN population expressing the transcription factor vsx2. Volumetric calcium imaging identifies two clusters of $vsx2^+$ neurons in the retropontine region and caudal medulla that are recruited at movement onset and are here termed Start/Maintain neurons. Optical backfilling reveals that neurons in both clusters project beyond the mid-spinal cord. To probe function, we combined visible holographic optogenetics with behavioral recordings to selectively stimulate a thin column of RSNs within these clusters. Brief unilateral activation within the retropontine Start/Maintain cluster, which has been implicated in both steering and forward locomotion, produced rapid large-amplitude ipsilateral tail bends, sometimes followed by tail oscillations. In contrast, the same unilateral stimulation in the caudal Start/Maintain cluster is sufficient to evoke sustained symmetric tail beats resembling forward swimming. Ongoing voltage imaging enables parallel recordings from over 100 $vsx2^+$ neurons during fictive locomotion, revealing distinct firing patterns between Start and Maintain neurons that are organized along the rostrocaudal axis. Single-cell morphologgical reconstructions support a model where retropontine Start neurons deliver descending signals to caudal medullary Maintain neurons, which in term sustain rhythmic activity through recurrent connectivity and spinal inputs. Together, these findings support a spatially organized reticulospinal circuit that transforms rostral initiation and steering signals into sustained motor drive in the caudal hindbrain.

Poster 8: Spinal circuits for locomotor adaptation

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Animals' ability to execute and adapt movements relies on neural networks in the spinal cord known as central pattern generators (CPGs), which regulate the rhythm and pattern of muscle contractions. CPGs include six neuronal populations, V0, V1, V2a, V2b, V3 and dI6, that differ in developmental origin, neurotransmitter phenotype and connectivity. Dysfunctions within these populations affect locomotor execution. We used an intersectional chemogenetic approach to transiently enhance (hM3D) or inhibit (hM4D) the activity of selected CPG populations and assessed the resulting changes in biomechanical strategies during motor tasks requiring either speed (treadmill) or postural adaptation (narrow beams). High-speed videos tracked with DeepLabCut were used to extract kinematic parameters from 15 body landmarks, while EMG recordings from flexor (tibialis) and extensor (gastrocnemius) muscles were used to infer kinetic features. Activation of V2a neurons shortened the stride and induced a crouched posture, conversely silencing of V2a neurons extended the stride and elongated the posture. Intriguingly, V2a activation also caused paw collisions and stuttering during beam, but not treadmill, locomotion. Preliminary EMG analyses suggest that V2a neuron activation, even on wider beams, increases flexor/extensor co-contraction, resembling the kinetic pattern observed during narrow beam locomotion. The paw collisions and muscle co-contraction driven by V2a activation, along with postural changes, suggest that these excitatory neurons are critical for real-time processing of proprioceptive feedback during demanding locomotion. Together, these findings indicate that V2a neurons promote adaptive biomechanical strategies during locomotion and may play a key role in integrating proprioceptive feedback during posturally demanding tasks.

Poster 9: Symmetry break and leg specific roles during curve walking in Drosophila

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When walking animals change directions, the motor system must break symmetry and generate differences in stepping kinematics between left and right legs. To understand these, we analyzed videos of free-walking flies, and induced curve walking. We found three major strategies to produce directional changes: adjustments, arcs, and turns. Adjustments arise from fast kinematic local changes on one step of the inner hind leg (HL) of the curve. Arcs comprehend several steps at constant speed and angular velocity, while turns are generated with fewer steps, and before execution flies decrease their speed. We found common kinematic lateral asymmetries between arcs and turns, such as slightly shorter swings and longer stances for middle leg (ML) and HL, and shorter stances for all inner legs, that become stronger in turns. Curve walking not only requires breaking the lateral kinematic symmetry, but also leg specific strategies are recruited sequentially when angular velocity increases. During arcs, the (1) outer stance amplitudes increase while (2) insider decrease, (3) Posterior Extreme Positions from outer front leg (FL) move away from the body and towards it for inner FL and ML. In addition, for turns (4) inside FL shift their Anterior Extreme Positions away from the body, (5) inner HL shortens the steps or (6) skips some, serving as pivot point, and in extreme cases (7) FL and ML generate lateral steps, and (8) inner HL and ML generate backward steps. This indicates that curve walking kinematics do not just display side-specificity, but leg specificity neural control.

Poster 10: A serotonergic sensory-gating pathway for adaptive locomotion

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Serotonin (5-HT) is a key neuromodulator of spinal locomotor circuits, but the identity and functional contribution to behavior of the serotonergic neurons underlying this modulation remain poorly defined. A longstanding hypothesis posits that serotonin influences locomotion by shaping sensorimotor processing, an essential determinant of adaptive movement. Here, we selectively target midline serotonergic neurons of the caudal raphe (CR^{5HT}) in mice to dissect their connectivity and function across spinal circuits and locomotor behaviors. Optogenetic activation of CR^{5HT} neurons in an ex vivo newborn brainstem-spinal cord preparation fails to recruit lumbar motoneurons but robustly suppresses motoneuron responses to sensory stimulation, suggesting a role in sensorimotor -gating. Consistent with this, CR^{5HT} projections in the adult lumbar spinal cord are enriched in the dorsal horn, a core hub for somatosensory integration. To determine whether this modulation impacts motor output, we manipulated CR^{5HT} activity in vivo during both spontaneous and skilled locomotion. While CR^{5HT} activation or silencing does not initiate (nor arrests) locomotion nor alters overall mobility in open-field conditions, they both significantly impair paw placement accuracy during horizontal ladder walking. Finally, retrograde trans-synaptic tracing uncovers a restricted set of direct presynaptic inputs to CR^{5HT} neurons from discrete brainstem and midbrain regions. Together, these findings identify CR^{5HT} neurons as a dedicated serotonergic pathway for sensory information processing that is required for precise, adaptive locomotion.

Poster 11: Cortical encoding of aversive-appetitive motivated locomotor movement

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Locomotion is fundamental for survival. Locomotion can be motivated by memories of previous rewarding or aversive experiences. The premotor cortex is widely implicated in movement planning, particularly for cue-driven, goal-directed actions. In mice, the secondary motor cortex (M2), is considered a premotor-like area that integrates task-relevant sensory information to drive skilled movements. However, the specific contribution of M2 in the planning of motivated locomotion, and how motivationally-driven locomotion is represented in the premotor circuits remains unclear.

Here, we combined an instrumental behavioral paradigm where auditory cues triggered appetitive or aversive motivated locomotion with single-cell resolution calcium imaging of M2 neuronal populations in unrestrained mice, to examine the encoding of motivated locomotion within this area. Mice were trained to discriminate three auditory cues: (1) a cue signaling locomotion to avoid an aversive foot shock (aversive motivation), (2) a cue signaling locomotion to obtain a reward (appetitive motivation), and (3) a cue signaling that locomotion would result in a foot shock if performed. Detailed video-tracking analyses were used to estimate locomotion onset times, revealing a consistent sequences of behavioral motifs preceding movement initiation. Preliminary analyses indicate that the encoding of motivated locomotor actions in M2 depends on the motivational valence of the instructive auditory cue, and that the activity of individual neurons can predict the initiation of motivated locomotion. These results provide a framework to dissect the neurobiological underpinnings of cue-driven motivated locomotion, and clarify the involvement of high-order premotor cortical areas in this process.

Poster 12: Spatial transcriptomics reveals distinct molecular signature of motor neurons and interneurons in control and pre-symptomatic stages of an ALS mouse model

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Amyotrophic Lateral Sclerosis (ALS) is a rapidly progressive and fatal neurodegenerative disorder impacting motor neurons (MNs) in the brain and spinal cord and resulting in muscle denervation and wasting. Evidence from SOD1G93A mouse model of ALS, carrying missense mutations in SOD1 gene, showed that inhibitory inputs (V1 En1+ interneurons) in the spinal cord are lost as early as pre-symptomatic stages of the disease and prior onset of MNs degeneration thus drawing attention at their putative role in disease. We thus uncovered the molecular signature of V1 En1+ interneurons (INs) and MNs using spatial transcriptomics. Spinal cord was dissected from WT and SOD1G93A mice at pre-symptomatic stages of disease (P45, P63 and P84) and processed for spatial transcriptomics using GeoMx Digital Spatial Profiler. At basal state, MNs display enrichment of cytoskeletal dynamics and transport-related targets. INs, on the other end, preferentially express genes involved in RNA splicing, mitochondrial organization and neurotransmission. Across early timepoints of disease, MNs present higher downregulation opposite to the biased upregulation observed in INs. Furthermore, a drastic drop in differential expression changes is observed in INs at P84 hinting at their premature loss. Metabolic, transport and synaptic transmission processes are similarly dysregulated in MNs and INs across disease timepoints. However, downregulation of synaptic targets (Snap25, Stxbp1, Unc13a) is preferentially observed in INs compared to MNs at pre-symptomatic stages of disease, suggesting early loss of connectivity between INs and MNs in ALS. Further investigation will be conducted to establish the impact of these changes in disease progression.

Poster 13: Corticospinal Connectivity after Developmental Damage: Circuit Plasticity & Functional Outcomes

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Spinal cord injury (SCI) disrupts corticospinal circuitry, among other circuits, and results in persistent motor deficits. The extent to which *developmental* injury of this circuit causes functional deficits in rodents remains poorly understood. The Sahni lab has established a novel microlesion approach and have demonstrated that corticospinal tract (CST) axons maintain their ability for axon extension after a developmental axotomy, for a brief developmental window. I aim to investigate the consequences of developmental axotomy of the CST with the goal of eventually applying these biological insights toward circuit function and dysfunction after adult injury. My current objectives are two-fold: first, determine how spinal connectivity is altered after a developmental lesion using a combination of transgenic mice, transsynaptic labeling and single nucleus RNA sequencing. Second, determine whether there are any behavioral consequences as a result of the developmental axotomy. Toward the second goal, I have developed behavioral biomarkers that can detect the developmental loss of CST connectivity. For this I have used a conditional knockout of *Fezf2* which results in a complete lack of specification of layer 5 extratelencephalic (L5 ET) neurons in the cortex. I find that this developmental loss of the CST leads to deficits in hindlimb control in adult cKO mice. Notably, these impairments emerge over time, highlighting the importance of longitudinal analyses in uncovering circuit-level dysfunction. Collectively, my work merges fundamental developmental and regenerative neuroscience to gain insight into basic mechanisms of circuit rewiring and functional recovery after injury.

Poster 14: AutoGaitA: A versatile quantitative framework for kinematic analyses across species, perturbations and behaviours

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Distinct behaviours require the nervous system to execute specialised motor programs, i.e., pre-structured patterns of muscle contractions, with characteristic sequence, timing, and force, which lead to specific reflexive or goal-oriented movements, e.g., forward walking, or backward swimming. Importantly, whether the execution and adaptation of these motor programs follow conserved principles across species and perturbations remains unclear. This is partly due to the lack of a standardised tool for such analyses. Although advances in deep-learning methods, such as DeepLabCut and SLEAP, have considerably improved motor assessments by facilitating the tracking of body landmarks across behavioural tasks and species, no universal framework exists to coalesce the generated time-stamped body coordinates into meaningful representations of motor programs. To provide standardised comparisons of motor programs across species, perturbations and behaviours, we developed the Python toolbox AutoGaitA (Automated Gait Analysis), which generates robust kinematic assessments of any limbed species performing any rhythmic behaviour of interest. Adopting AutoGaitA for a cross-species walking paradigm, we found that locomotor programs in flies, mice, and humans rely on diverse mechanisms to generate limb propulsive strength, but employ a similar distal-to-proximal gradient of joint movement velocities. Also, we showed that ageing induces a loss of propulsive strength in all species while preserving the velocity gradient. Furthermore, we observed that in mice, locomotor programs adapt as an integrated function of concomitant perturbations, namely ageing and task difficulty. Thus, with AutoGaitA, we began to reveal the conserved and divergent mechanisms underlying the execution of locomotor programs in physiological and perturbed states.

Poster 15: Identification of CSF-contacting neurons subtypes in the mouse spinal cord

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The capacity for voluntary movement is the defining feature of animals. From postural adjustment to complex locomotion, adaptive motor control requires precise information about body position and movement that is generated by integrating multiple streams of sensory feedback. Cerebrospinal fluid-contacting neurons (CSF-cNs) represent a unique population of intraspinal chemo- and mechano-sensory neurons that are conserved across vertebrate evolution. Although growing evidence supports an important role for CSF-cNs in control of swimming in lamprey and fish, it remains unclear how this ancient system has evolved and adapted for limbed-based movement in mammals. To start addressing this question we investigated the molecular diversity of mouse CSF-cNs. Because CSF-cNs are typically underrepresented in whole spinal cord datasets, we generated a dedicated snRNAseq dataset by using genetic labeling and isolation of CSF-cNs nuclei from neonatal pups. We identified five molecularly distinct CSF-cNs subtypes. Beyond known markers, we detected additional subtype-associated genes suggesting greater cell-fate diversity of CSF-cNs than previously recognized. In vivo validation revealed robust spatial patterning along the rostrocaudal and dorsoventral axes corresponding to molecularly distinct clusters. Importantly, several subtypes exhibited partially overlapping transcriptional profiles, consistent with a developmental continuum in which some clusters seem to reflect different states of maturation rather than terminally differentiated subtypes. Future work will extend this atlas across postnatal development and combine genetic targeting to link molecular identity to circuit integration and functional roles. Overall, our results indicate the existence of molecularly and anatomically distinct subtype of mammalian CSF-cNs providing a framework for further mechanistic and functional studies.

Poster 16: Disrupted cAMP dynamics in the secondary motor cortex during sensorimotor and motor learning behaviour in the R6/1 mouse model of Huntington's disease

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Huntington's disease (HD) is a hereditary neurodegenerative disorder caused by an expanded CAG repeat in exon 1 of the HTT gene, leading to progressive motor, cognitive, and psychiatric impairments. A hallmark of HD pathology is the gradual dysfunction of the cortico-striatal pathway, accompanied by alterations in intracellular signalling cascades, including disrupted cAMP signalling, which may contribute to impaired neuronal plasticity. Here, we investigated neuronal cAMP dynamics in the R6/1 mouse model of HD during behavioural tasks that depend on M2 cortical function. To this end, we expressed the fluorescent cAMP sensor GFlamp1 (AAV9-hSyn-Gflamp1-WPRE) in M2 cortical neurons of 8 week old mice and performed fiber photometry recordings during the Beetle Mania Task (BMT; 14 and 20 weeks) and the accelerated rotarod (ARR; 14–15 weeks). Baseline corrected ΔF/F (z score) signals revealed robust increases in cAMP levels in response to beetle exposure during the BMT. However, these responses were significantly blunted in HD mice at 20 weeks, but not at 14 weeks, relative to wild-type littermates. This reduction was particularly evident in males, which showed decreased peak amplitude and AUC, while females remained unaffected. During the ARR, cAMP levels also rose upon task engagement. Although baseline levels did not differ between genotypes, female wild-type mice exhibited higher cAMP responses than HD females during the stimulus phase, an effect that was even more pronounced after task completion in the home cage. Altogether, these findings demonstrate task related increases in neuronal cAMP levels and support a role for altered cAMP signalling in HD pathophysiology.

Poster 17: Cortico-brainstem pathway compensates for loss of corticospinal output after stroke and spinal cord injury

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Descending cortical projections are essential for skilled motor control, and injury to these pathways results in substantial motor impairments. We recently identified parallel descending pathways arising from distinct subsets of subcerebral projection neurons (SCPN) that diverge during development: cortico-brainstem neurons (CBN), which limit axon extension to the brainstem, and corticospinal neurons (CSN), whose axons extend into the spinal cord while also innervating the brainstem. While compensatory sprouting of CSN has been linked to functional recovery after stroke and spinal cord injury (SCI), whether CBN undergo structural plasticity or contribute to recovery after such injuries remains unclear. Here, we investigated CBN axonal plasticity and their role in functional recovery following stroke and SCI. Specifically, we asked how spared CBN axons remodel their brainstem collateralization in response to two anatomically distinct insults: a cortical lesion caused by unilateral loss of SCPNs after stroke, and a spinal injury that disrupts corticospinal connectivity. Using StARQ, a machine learning-based pipeline for quantifying axonal collateralization across the entire rostro-caudal extent of the brainstem, we found that CBN axons exhibit increased collateralization in caudal brainstem regions in both injury models, regions that are usually dominated by corticospinal collaterals. Ongoing work will assess the functional relevance of this reorganization using skilled forelimb behavior combined with chemogenetic silencing of CBN. Overall, our results indicate that spared cortico-brainstem pathways are consistently recruited when direct corticospinal access to downstream motor circuits is compromised, positioning CBN as a flexible relay for cortical output after central nervous system injuries.

Poster 18: Exploring the role of the premotor trigeminal complex in masticatory function

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Masticatory movements are part of the more complex behavior of feeding. Similar to breathing and locomotion, known as a Central Pattern Generator (CPG), found within the brainstem, but it is assumed that their coordination with other movements during feeding occurs elsewhere. The boundaries of the CPG are known, but its organisation is less understood. Here we mapped, within these boundaries, areas activated during cortically evoked mastication, using c-fos immunostaining. Optogenetic stimulation of the cortical masticatory area (CMA) evoked rhythmic jaw movements (RJMs), and increased activity in the trigeminal main sensory nucleus (NVsnpr), and in regions medial (JuxtV) and ventral (PCRt) to the trigeminal motor nucleus. Optogenetic stimulation of JuxtV and PCRt in head-fixed awake animals produced some uncoordinated jaw movements. In contrast, stimulation of NVsnpr induced robust RJMs, and some hand-to-mouth movements resembling those occurring during natural feeding and food manipulation, raising the intriguing possibility that complex behaviors may be partly encoded at the CPG level. We have previously shown that NVsnpr neurons shift their firing pattern from tonic to rhythmic bursting when the extracellular Ca2+ concentration is decreased by release of S100β, an astrocytic Ca^{2+}-binding protein. Here, we show that S100β levels increase in NVsnpr during CMA-induced RJMs, while injection of an anti-S100β antibody delays these movements. A selective Nav1.6 blocker (4,9-anhydroTTX), acting on the conductance modulated by S100β, also greatly reduced the frequency and amplitude of cortically induced RJMs. These results will help resolve the composition of the masticatory CPG and establish the role of astrocytes in rhythmogenesis.

Poster 19: Gene expression mapping of the mesencephalic locomotor region, reticular formation and spinal motor circuits in larval zebrafish

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Locomotion is essential to animal behaviors enabling them to explore, hunt, or escape from predators. In vertebrates, voluntary locomotion relies on the recruitment of the mesencephalic locomotor region (MLR), which provides inputs to command neurons called reticulospinal neurons (RSNs). RSNs, in turn, transmit descending commands to locomotor central pattern generators (CPGs) in the spinal cord. Motor output is ultimately produced by spinal motor neurons and premotor interneurons, whose genetic identities are well established during embryonic development through conserved transcription factor programs. While this transcriptional code has been extensively characterized across species in the spinal cord, the genetic make up of motor circuits in the brainstem remains much less understood. To bridge this gap, we analyze the expression of an array of molecular markers ranging from neurotransmitters, neuromodulators, peptides, and their receptors that are involved in modulating the activity of locomotor circuits. We use hybridization chain reaction RNA-fluorescent in-situ hybridization (HCR RNA-FISH) combined with all brain imaging, to systematically map these markers and reconstruct the position of labelled neurons in the brainstem and spinal cord of 5-6 day old larval zebrafish. Together, this effort allows us to build a comprehensive atlas of gene expression in key brainstem and spinal motor centers, and will open the possibility to refine genetic targeting of motor circuits in vivo as well as assessing gene expression conservation across species.

Poster 20: Contribution of striatal D1-expressing neurons to motor deficits in early and late stages of the Huntington's disease

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Huntington's disease (HD) is a progressive neurodegenerative disorder in which basal ganglia dysfunction underlies motor deficits. The striatum integrates cortical and thalamic glutamatergic inputs and relays them via direct and indirect pathways. Direct pathway medium spiny neurons (dMSNs; Drd1-expressing) facilitate movement through transient inhibition of GPi and SNr and are altered in HD. Here, we aim to investigate how Drd1 expressing striatal neurons show dynamic functional alterations during behaviour across pre symptomatic and symptomatic stages of HD. Using in vivo fibre photometry, we recorded calcium dynamics in dMSNs during defined behavioural tasks. R6/1 Drd1a Cre+/− mice (Drd1 HD) and WT Drd1a Cre+/− controls (Drd1 WT) received stereotaxic injections of AAV flex GCaMP6f into the dorsal striatum at 8 weeks (early stage) or 16 weeks (later stage), followed by unilateral implantation of a fibre optic cannula. Behavioural assessment included the Beetle Mania Task (BMT), probing approach and defensive responses to an unexpected visual stimulus, and the accelerated rotarod, evaluating motor learning at 12 and 20 weeks of age. In the pre-symptomatic phase, HD and WT mice show similar rotarod performance, with increased latency to fall across trials. Calcium signals rise upon placement and return to baseline within seconds before the fall, with no genotype differences. However, in the symptomatic phase, HD mice show impaired rotarod performance (reduced latency to fall), with a larger initial Ca^{2+} rise and faster decay than WT. In contrast, Drd1-expressing neurons exhibit similar calcium responses in WT and HD mice during the BMT at both pre-symptomatic and symptomatic stages. Together, these findings reveal that the direct pathway shows dynamic alterations, measured as calcium fluorescent changes, dependent on the stage of the disease and on the behavioural task.

Poster 21: Modelling the Emergence of Asymmetric Motor Deficits in Amyotrophic Lateral Sclerosis Using a Bilateral Spinal Central Pattern Generator

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Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease characterised by progressive degeneration of motor neurons and spinal interneuron populations. Early disease symptoms often emerge asymmetrically, with weakness appearing first in one limb before spreading to the contralateral side. Although lateralised onset is well documented in patients and SOD1 mouse models, the circuit-level mechanisms underlying this asymmetry remain poorly understood. Here, we develop a computational modelling framework to investigate how asymmetric degeneration within spinal locomotor circuits can generate lateralised motor dysfunction. We construct a bilateral mammalian spinal central pattern generator (CPG) comprising reciprocally coupled flexor–extensor rhythm generators, ipsilateral interneuron populations (V1, V2a, V2b, V0c, Renshaw and Ia pathways), and commissural interneurons (V0d, V0v, and V3 subtypes) responsible for interlimb coordination. The model is implemented using the NEST simulation environment to generate rhythmic spinal network dynamics informed by experimental and computational literature. Network activity is quantified using oscillation frequency, burst duration, firing rates, and phase relationships between flexor–extensor and left–right populations. We test degeneration paradigms simulating selective vulnerability of inhibitory interneuron classes. We hypothesise that unilateral loss of V1 and V2b inhibitory interneurons is sufficient to disrupt locomotor timing, weaken commissural coupling, and drive lateralised motor deficits. Preliminary simulations demonstrate that asymmetric interneuron degeneration produces altered burst timing, reduced rhythmic stability, and phase desynchronisation between bilateral CPG outputs, recapitulating early-stage ALS-like motor patterns. This work provides a mechanistic framework linking circuit-level asymmetry to disease progression and highlights potential therapeutic targets for stabilising locomotor network function.

Poster 22: Intrinsic properties of external globus pallidus neurons in dopamine depleted mice

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Parkinson´s disease (PD) is a neurodegenerative disorder associated with the loss of midbrain dopaminergic neurons in the substantia nigra pars compacta and their projections in the basal ganglia (BG). The globus pallidus externa (GPe) is a central part of the BG that is affected by dopamine loss. It is composed of two subpopulations that differ in terms of electrophysiological properties, molecular markers, and targets. The majority of GPe cells are called prototypic neurons, which are highly active, while the arkypallidal neurons are a smaller group of less active cells projecting to the striatum. In this study, we characterized the intrinsic properties and intrapallidal connectivity of the subpopulations and their alteration in the unilateral 6-hydroxydopamine model of PD in mice using the ex-vivo slice preparation. We found that both types of neurons showed reduced excitability following dopamine depletion. Specifically, we report that the prototypic cells of dopamine-depleted mice display reduced input resistance and increased rheobase compared to dopamine-intact animals. Arkypallidal cells in dopamine depleted mice showed decreased membrane potential and increased rheobase, as well as decreased action potential amplitude and half-width compared to controls. Recording the membrane properties of GPe cells in the presence of synaptic transmission blockers revealed that changes in excitability may be partially attributed to changes in synaptic input strength. Our results thus point towards a combined effect of intrinsic and synaptic mechanisms underlying the reduced excitability in the GPe neurons in a cell-type-specific manner following dopamine depletion. Deciphering these mechanisms could enable better treatment for PD.

Poster 23: Circuit-level mapping of locomotor network recruitment during neuromodulatory stimulation after spinal cord injury

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Spinal cord injury (SCI) often results in locomotor impairments, yet substantial supraspinal pathways can remain structurally intact, representing promising targets for functional recovery. Midbrain locomotor regions, including the cuneiform nucleus (CnF), are increasingly explored as entry points to engage residual descending control and enhance rehabilitation outcomes. However, despite extensive work dissecting individual components of supraspinal and spinal locomotor control, how these circuits are integratively recruited across levels during locomotion, and how this distributed recruitment is reconfigured after SCI and neuromodulation, remain largely undefined. Here, we used activity-dependent genetic labeling in TRAP2 mice combined with quantitative locomotor profiling to map locomotion-related networks across defined behavioral conditions. Neurons were permanently tagged during periods of no movement, walking alone, or walking coupled with optical stimulation of the CnF, allowing discrimination between locomotor recruitment from stimulation-enhanced recruitment. Using this framework in intact and thoracic incomplete SCI mice, we mapped distributed activity-defined neuronal populations across supraspinal nuclei and spinal cord regions during locomotion and neuromodulatory stimulation. Together, this work establishes a circuit-level anatomical framework that enables future causal and mechanistic interrogation of activity-defined locomotor circuits, providing a foundation for mechanism-guided neuromodulatory rehabilitation strategies after SCI.

Poster 24: Interrogating deep brain stimulation circuit activity using focused ultrasound

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Ultrasound Localization Microscopy (ULM) extends functional ultrasound (fUS) to the microvascular scale by localizing circulating microbubble contrast agents, achieving near-capillary resolution and enabling quantitative microvascular flux mapping. Because microvascular flow reflects neurovascular coupling, time-resolved microbubble flux provides an indirect measure of neural activity and supports functional connectivity estimation. In rodents, functional ULM has demonstrated that flux dynamics encode neurovascular coupling and enable connectivity mapping. Translating this approach to non-human primates is a critical step, as primate cerebrovascular topology, flow regulation, and coupling dynamics more closely resemble human physiology. Compared with BOLD fMRI, fUS offers higher temporal resolution, improved microvascular specificity, and portable, lower-cost hardware. Within this framework, we aim to characterize deep brain stimulation (DBS) targets and their distributed networks in movement disorders, including Parkinson's disease and Essential Tremor. We seek to determine how these circuits are organized, how they operate under anesthetized and task-based conditions, and how they are modulated by DBS. We hypothesize that stimulation induces multi-timescale changes not only locally but across long-range networks, and that understanding these distributed effects will inform therapeutic refinement and future minimally invasive sonogenetic neuromodulation strategies. Whole-brain multi-slice 2D-ULM data were acquired in anesthetized squirrel monkeys using a research ultrasound system (6.25 MHz, 128-element probe, 250 × 250 μm² resolution) during 3-minute bolus injections (200 μL Bracco microbubbles + 200 μL saline), following Orset et al. (bioRxiv, 2025). ULM slices were co-registered to individual T2-weighted MRI using rigid affine alignment followed by demons nonlinear refinement in MATLAB. Backscattering amplitude enabled 3D microbubble localization within a common MRI space, from which mean flux was rendered as a 3D point cloud. The VALiDATe29 atlas was aligned to subject MRI via centroid pre-alignment, similarity refinement, and demons registration, and atlas labels were propagated to define gray matter regions of interest. Bolus phases were synchronized across slices using peak detection to align flux time series. Regional mean flux signals were extracted and functional connectivity matrices computed by correlating gray matter time courses. Preliminary results demonstrate successful 3D reconstruction, MRI co-registration, and preliminary functional connectivity mapping from vascular flux dynamics in three anesthetized squirrel monkeys. Next steps include assessing statistical significance and inter-animal reproducibility of connectivity patterns toward a fully integrated 2D fUS–MRI analysis framework. This platform enables systematic investigation of DBS-induced network modulation in non-human primates.

Poster 25: Input and Output Connectivity Matrix of Chx10-PPN Neurons Involved in Pause-and-Play Behavior

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Locomotion is an essential and conserved movement that allows humans and animals to interact with their surroundings. Although locomotion appears seemingly effortless, it is an intricate motor behavior that requires the orchestration of several supraspinal and spinal neuronal substrates to activate many axial and limb muscles. This enables organisms to navigate through and adapt to their environment. Such context-dependent and episodic locomotor behaviors necessitate an interruption or arrest to adjust the movement toward a specific goal. However, the neural pathways for motor arrest behaviors in response to significant environmental changes—beyond fear-related and defensive contexts—are poorly understood. Recently, Goñi-Erro H. et al., Nat Neurosci, 2023, discovered a population of glutamatergic neurons in the rostral pedunculopontine nucleus (PPN) expressing Chx10, which evokes a unique whole-body motor arrest, characterized by a pause-and-play behavior as well as apnea and bradycardia. However, the functional involvement of upstream and downstream brain areas to the described behavior remains largely unknown. To reveal this, we first took advantage of recent rabies virus-based monosynaptic tracing tools and identified distinct presynaptic input neurons to Chx10-PPN neurons in prefrontal areas, hypothalamus, and subthalamus. Second, we used anterograde and retrograde tracing to identify postsynaptic neurons predominantly in the caudal brainstem and assessed their functional involvement in the motor arrest. Together, this work provides insights into the neuronal mechanisms governing context-dependent selection of arresting motor behaviors, linking those motor outputs to cellular activities and advancing our understanding of how the nervous system orchestrates complex motor actions.

Poster 26: Subthreshold oscillations of preBötzinger Complex VGluT2+ neurons enable instantaneous modulation of inspiratory rhythm generation in vivo

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Breathing is a vital motor behavior that must remain robust to sustain life while retaining flexibility to accommodate changing physiological and behavioral demands. This adaptability requires the breathing central pattern generator (bCPG) to operate across multiple dynamic modes in response to sensory, emotional, cognitive, and motor inputs. The preBötzinger Complex (preBötC) in the ventral medulla controls the generation of breathing rhythm and pattern and serves as the core kernel of the bCPG for eupneic breathing and its modulated forms, such as sniffing and sighing. We identify subcritical network oscillations, termed "burstlets", in the preBötC in vivo in mice as a fundamental dynamical feature of the bCPG that enables flexibility within an otherwise robust rhythm. In vivo electrophysiological recordings reveal burstlets occurring at higher harmonics of the breathing frequency, and fiber-optic calcium imaging demonstrates that these rhythmic burstlets are generated by the excitatory preBötC VGluT2+ neurons. Circuit perturbations using ultrapotent inhibitory DREADDs further show that excitatory VGluT2+ neurons generate both burstlets and inspiratory bursts in vivo, while GlyT2+ neurons provide feedback inhibition that regulates excitation-inhibition balance, a key determinant of burstlet propagation and transitions between breathing modes. Importantly, we provide evidence for two distinct mechanisms of breathing rhythm modulation: (i) a slow and continuous mechanism that engages rhythmogenic neuronal populations to set the intrinsic frequency of burstlets, (ii) and a fast and quantal mechanism that operates without directly altering activity of rhythmogenic neurons and instead determines which burstlets are converted into inspiratory bursts, thereby producing rapid state transitions in motor output. Consistent with this framework, increasing lung inflation in anesthetized mice produced quantized slowing of breathing rhythm, while selective excitation of non-rhythmogenic populations evoked transient increases in rhythm resembling sniffs that occurred at integer multiples of baseline frequency; in awake mice, stimulus-evoked sniffs were similarly quantized relative to baseline breathing. Together, these findings support a dynamical framework in which neuromodulatory and sensory inputs exploit preBötC subcritical oscillations to enable rapid and flexible transitions between breathing motor states, providing a mechanistic basis for adaptive control of a vital motor behavior.

Poster 27: Non-volitional slow breathing training produces persistent reductions in anxiety and stress reactivity via the preBötzinger complex

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Breathing is a vital motor behavior generated by the brainstem central pattern generator (CPG) circuits that must remain robust while retaining flexibility to adapt to behavioral and physiological demands. Volitional slow breathing in humans reduces anxiety and stress, yet the mechanisms underlying these effects remain unclear and are difficult to dissect due to cognitive and placebo influences. To isolate the contribution of breathing itself, we developed a murine model in which breathing rate is experimentally slowed without volitional control by selectively manipulating inhibitory neurons in the preBötzinger Complex (preBötC), the core rhythmogenic kernel of the mammalian breathing CPG. Repeated episodic slowing of breathing (30 min/day for 4 weeks) in awake mice produced sustained reductions in breathing frequency during training sessions without impairing the ability to generate high-frequency breathing. Importantly, prior experience with slow breathing markedly reduced anxiety-like behavior and stress-enhanced fear responses measured days after training, despite no concurrent manipulation of breathing during behavioral testing, indicating persistent changes in state rather than acute respiratory effects. These findings demonstrate that experience-dependent modulation of a brainstem motor pattern can induce long-lasting changes in behavioral responses to stress, revealing a causal bottom-up pathway linking respiratory motor circuits to emotional state regulation. This work establishes an experimental platform for mechanistic investigation of how modulation of a fundamental motor rhythm influences brain-wide function and behavior.

Poster 28: Investigating the Early Frontotemporal Dementia Phenotypes in a Mouse Model of TDP-43 Proteinopathy

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Frontotemporal dementia (FTD) is a fatal neurodegenerative disorder affecting the frontal and temporal lobes, with the behavioural variant of FTD being characterized by social impairment, changes to personality and affective processing, and executive dysfunction. FTD and amyotrophic lateral sclerosis (ALS) exist along a shared disease spectrum, with 30–50% of patients displaying both cognitive and motor symptoms, and the majority of ALS-FTD cases exhibit TDP-43 pathology. This study employs a tetracycline-repressible TDP-43 mouse model that replicates ALS-FTD pathology across neurons, demonstrating motor impairment, brain atrophy, and reversible disease progression. This work examines cognitive alterations during the early stages of ALS-FTD.

Here, FTD-like phenotypes were assessed using behavioural paradigms measuring activity, exploration, anxiety, memory, and sociability. Mice were tested at three timepoints: pre-induction, one week, and two weeks post-induction. Behavioural analyses revealed hyperactivity, reduced sociability, and altered anxiety-like behaviour. Unsupervised machine learning was applied to detect subtle behavioural changes, identifying reduced behavioural motifs such as standing still and sniffing, alongside increased locomotion, turning, and rearing across paradigms. These findings indicate hyperactivity, altered exploratory patterns, and emerging stereotypic behaviours. In addition, anatomical analyses suggest changes in interneuron populations within the medial prefrontal cortex at the same timepoints. Ongoing fibre photometry experiments are investigating functional alterations in interneuron activity associated with these behavioural changes. In conclusion, we identified milder, clinically relevant early-stage phenotypes that recapitulate FTD symptoms and with potential to study system-level effects of TDP-43 expression.

Poster 29: Encoding fine-grained forelimb movements through molecularly heterogeneous brainstem neurons

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Movement control is an inherently multifaceted problem, engaging a multitude of structures across the brain. Brainstem neurons, with their unique anatomical location proximal to motor output, their activity being highly correlated with movement execution and their potency to generate movements upon stimulation, play an important role in movement generation. Here we focus on the lateral rostral medulla (latRM), the brainstem hub for the control of forelimb movements, and address how the diverse excitatory latRM neurons, as characterized by their molecular underpinnings and synaptic connectivity, together encode diverse forelimb movements. We employ both high throughput (Neuropixels) and cell type specific (2-photon miniscope) neuronal recording in the latRM of freely moving mice, performing a pellet reaching task or innate forelimb behaviors. We found that excitatory latRM neurons encode a basic set of fine-grained forelimb movements, such as arm extension or supination, that are sequentially recruited in different behaviors, such as pellet reaching and grooming, suggesting that latRM neurons encode movements in a behavior-context independent manner. Clustering latRM neurons into functional types based on their activity around selected movement timestamps, we found that functional types exhibited distinct modulation patterns to specific forelimb movements. Strikingly, employing single-cell RNA sequencing and spatial transcriptomics, we found that excitatory latRM neurons also stratify into many molecularly defined and spatially organized subpopulations. To address how latRM functional types map onto these molecular types, we identify the same neurons from in vivo calcium imaging and from confocal imaging for post-hoc molecular identification. These experiments yield accumulating evidence of a correspondence between functional and molecular cell types in brainstem forelimb movement generating circuits. Our study not only extends our understanding of brainstem circuits in movement generation but also provides a theoretical basis for the investigation of other important nodes in the motor system.

Poster 30: Midbrain input regulates motor thalamic reticular nucleus activity during skilled forelimb movement

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Movement relies on coordinated activity across distributed brain networks that link subcortical structures and cortex. The motor thalamus occupies a central position in these networks, and its activity is shaped by inhibition from the thalamic reticular nucleus (TRN), a GABAergic shell that provides topographically organized input to thalamic nuclei. While communication principles between thalamocortical centers and the TRN have begun to be unraveled, how TRN circuits contribute to motor control remains largely unknown. Here, we leverage circuit tracing strategies in mice to delineate the motor sector of the TRN. Recordings from identified motor TRN neurons during a skilled forelimb task revealed movement-correlated changes in its firing rate. Optogenetic perturbation of this activity disrupts ongoing movement, demonstrating the important role of this circuitry in forelimb control. To identify inputs that might contribute to these movement-specific activity changes, we mapped afferents to the motor TRN. We uncovered a prominent inhibitory midbrain source that provides topographically organized synaptic input selectively to this sector. This midbrain pathway acts as a hub, integrating signals from multiple motor-related regions and positioning it as an integrative node upstream of the motor TRN. Electrophysiological recordings during behavior show that this midbrain–TRN pathway and motor TRN neurons undergo complementary activity changes during forelimb movement, consistent with temporally coordinated circuit dynamics. Our findings offer new insight into the organization and function of synaptic inputs to the motor TRN and highlight the contribution of a previously uncharacterized inhibitory input to the TRN within the broader thalamocortical network during skilled forelimb movement.

Poster 31: Cerebrospinal Fluid Noradrenergic Signaling Sustains Motor Arrest through Disruption of Motor Commands

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Neuromodulators can mediate whole-body physiological changes, however how signaling from relatively small populations of neurons produces widespread and sustained effects remains incompletely understood. Here, we demonstrate that sustained noradrenergic activation induces prolonged motor arrest accompanied by postural collapse, bradycardia, and emetic responses. Noradrenaline induces a glial calcium wave that propagates throughout the central nervous system. This wave most prominently persists at the brainstem-spinal cord boundary and ventricular midline. At this location, ependymal radial glia express Adra1a receptors on cilia contacting cerebrospinal fluid (CSF). Ventricular noradrenaline injections recapitulated the glial wave and motor arrest, while CSF administration of an Adra1 antagonist shortened motor arrest. Motor suppression arises from inhibition of brainstem commands to the spinal cord rather than motoneuron silencing. Altogether, noradrenaline sustains long-lasting disconnection from brain to spinal cord by signaling through the CSF via ciliary Adra1a receptors on ependymal radial glia. This establishes cerebrospinal fluid as a critical transmission route for persistence of behavioral states.

Poster 32: Neuronal activation mapping in the spinal cord following high-intensity trans-spinal magnetic stimulation in mice

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Trans-spinal magnetic stimulation (TSMS) is a promising non-invasive neuromodulation approach for spinal cord injury (SCI). In our laboratory, high-intensity repetitive TSMS (HI-rTSMS) has demonstrated therapeutic benefits after SCI. However, the acute cellular mechanisms underlying these effects remain poorly understood. The direct impact of HI-rTSMS on spinal neuronal activation has not yet been clearly characterized. Here, we investigated early neuronal responses following a single session of HI-rTSMS in healthy mice. HI-rTSMS (0.4 T, 10 Hz) were delivered using a human-sized circular coil according to a patterned protocol consisting of 10 s stimulation followed by 20 s rest, repeated over a total duration of 10 minutes. Three-dimensional spatial mapping of the magnetic field was performed to characterize the stimulation profile. Mice were anesthetized under isoflurane during stimulation. To evaluate the influence of post-stimulation behavioral state, animals either remained anesthetized or were allowed to wake for one hour prior to perfusion, corresponding to the peak window of c-Fos expression.

Spinal cords were collected and processed for immunohistochemistry using DAPI, NeuN, and c-Fos. Neuronal activation was quantified as $c\text{-}Fos^{+}/NeuN^{+}/DAPI^{+}$ cells, allowing analysis of dorsal and ventral spinal cord regions. In anesthetized animals, HI-rTSMS induced a significant reduction in neuronal activation compared to non-stimulated controls, suggesting an acute inhibitory or modulatory effect. In contrast, awake mice showed no significant difference in c-Fos expression between conditions.

This study provides a spatially informed analysis of spinal neuronal activation following HI-rTSMS and highlights the importance of animal state when interpreting acute neuronal effects.

Poster 33: Study of oligodendrocytes degeneration and study of transspinal repetitive magnetic stimulation in sod1 mouse model of ALS

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Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease characterized by the degeneration of neurons from the motor cortex and motoneurons in the brainstem and spinal cord, leading to paralysis and death within 2–5 years of diagnosis. Current treatments are limited: riluzole modestly extends survival, and tofersen (QALSODY®) targets only patients with the SOD1 mutation. Neuronal degeneration in ALS involves both cell-autonomous processes, due to intrinsic neuronal dysfunction, and non-cell-autonomous mechanisms driven by glial cells. Astrocytes and microglia involvement are well studied. In contrast, the role of oligodendrocytes is less understood, though existing studies suggest they significantly contribute to motoneuron degeneration. This study investigates oligodendrocyte involvement in ALS pathophysiology and evaluates repetitive transspinal magnetic stimulation (rTMS) as a non-invasive therapy to improve motor function in the SOD1 mouse model. Previous work in the lab demonstrated that rTMS reduces neuronal death, demyelination, and inflammation, while promoting locomotor recovery in models of spinal cord injury. From a physiopathological standpoint, we show that disease progression is associated with a decrease in the proportion of mature oligodendrocytes and a concomitant increase in oligodendrocyte progenitor cells in the ventral horn of the lumbar spinal cord, beginning at P50. From a preclinical perspective, we further demonstrate that a 14-days rTMS treatment restores these cellular proportions to WT levels and preserves motoneuron integrity. These findings suggest that oligodendrocytes play a critical role in ALS progression and that rTMS may offer a promising therapeutic strategy to delay the onset and/or the progression of the disease.

Poster 34: Fight, Flight, and Firing: Investigating the Effects of Aversive Stimuli on Glutamatergic Cell Activity in the Medial Zona Incerta

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It has been established that context-specific locomotor behaviours are controlled by brain regions that respond to internal and external cues, which are then translated to the brainstem to execute a movement. However, the integration of these higher command centres with downstream brainstem locomotor areas is not well understood. One such higher brain region is the medial zona incerta (mZI), a critical subcortical region for sensorimotor integration and creating complex locomotor behaviours. Our previous work shows that the mZI contributes to the contextual control of movement. Here, I examined the activity of mZI glutamatergic neurons using a battery of behavioral tests. vGLUT2-Cre mice (n=20, 10 female/10 male) were injected with Cre-dependent AAV-GCaMP8. Ca2+ transients from mZI vGLUT2 neurons were recorded using fiber photometry from freely moving mice during an array of behavioural tests (open field, hole board, elevated plus maze, looming shadow test, air puff, aversive noise, and footshock). In male mice, glutamatergic mZI activity increased significantly with the onset of air puff, aversive noise, and footshock stimulations. The increase in glutamatergic mZI activity suggests that the mZI is involved in responding to aversive stimuli. My next step is to explore sex differences in glutamatergic mZI activity and behavioural responses to aversive stimuli, and directly examine neuronal activation using activity-dependent markers. This will confirm whether glutamatergic mZI populations are activated by specific stimuli, in a sex-dependent manner.

Poster 35: Modular V2a reticulospinal circuits orchestrate distinct kinematic strategies for turning

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Turning, the ability to change locomotor direction, is essential for animals to navigate their complex environments. Yet, unlike straight-ahead locomotion, its kinematics and neuronal control remain poorly understood, reflecting both the historical lack of tools for 3D tracking and the relatively recent identification of V2a reticulospinal neurons as key drivers of turning. To elucidate these aspects, we adapted a high-resolution motion capture system for mice to dissect the kinematic building blocks of natural turning, and to map the functional organization of V2a descending pathways potentially controlling them. Our 3D analysis of joint-specific rotations and stepping cycle revealed a rich repertoire of natural turning strategies, characterized by different combinations of asymmetric body-axis configurations, limb-specific gait asymmetries, and precise speed modulation. Strikingly, these motor components are independently governed by three distinct projection-specific V2a reticulospinal modules: V2a>C2–T13 neurons control head-to-tail body-axis alignment, V2a>L1–L4 neurons regulate locomotor speed, and V2a>L5–S2 neurons coordinate left-right gait asymmetries. Altogether, our findings define the core kinematic strategies for quadruped turning and reveal that their flexible orchestration arises from a modular V2a reticulospinal organization, thus providing a circuit-level framework for directional locomotor control.

Poster 36: Low-intensity magnetic stimulation exerts pattern-dependent effects on tissue repair after spinal cord injury

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Spinal cord injury (SCI) is a devastating condition leading to permanent sensorimotor deficits below the lesion site, associated with fibroglial scar formation, neural network disruption, and a chronic inflammatory environment. Effective treatments remain limited; nevertheless, neuromodulation has emerged as a promising strategy to enhance functional recovery and promote tissue repair after SCI. Among these approaches, repetitive magnetic stimulation (rMS) is a widely used therapy in humans that non-invasively modulates neural excitability and plasticity at both cortical and spinal levels. Previous studies have shown that trans-spinal rMS at high-intensity improves motor function and tissue remodeling in rodents. In this context, our study focuses on low-intensity rMS (LIrMS) and investigates how focal spinal stimulation patterns influence spinal cord repair after injury. Wild-type mice underwent SCI, followed by two weeks of either sham or trans-spinal LIrMS with three stimulation patterns. Locomotor recovery was assessed using the Basso Mouse Scale, and spinal cord samples were collected for immunohistochemistry and RNA sequencing. Our results indicate that LIrMS induces pattern-dependent effects on fibroglial scar reorganization, inflammatory processes, and myelin debris clearance. Transcriptomic profiling revealed distinct molecular signatures depending on the stimulation pattern, involving pathways related to fibrosis, immune and inflammatory regulation, vascular dynamics, and apoptotic processes. These data identify focal trans-spinal LIrMS as a promising neuromodulatory strategy to promote spinal cord repair, and pave the way for future investigations, including validation in a rat model whose pathophysiology after SCI is closer to humans.

Poster 37: Neurons exhibiting anti-motor activity in the Xenopus laevis tadpole hindbrain

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Neural circuits function in a state-dependent manner. For example, motor outputs to the same sensory input can vary depending on the animal's current behavioral state: sleep vs wakefulness, hunger vs satiety, movement vs rest. The mechanisms for locomotion initiation, maintenance and cessation have been studied extensively. In contrast, neurons active at rest and those involved in inducing and maintaining a state of immobility remain poorly understood. Previous whole-brain imaging experiments identified cell clusters in the Xenopus laevis tadpole hindbrain exhibiting anti-motor activity i.e., activity negatively correlated with fictive locomotion. To investigate this further, we employ single-cell calcium imaging, whole-cell patch-clamp electrophysiology and anatomical staining to study these cells' activity, synaptic inputs, morphology and potential roles in motor/behavioral state control. Using GCaMP6s calcium imaging, we find cells in the ventral-rostral hindbrain with high baseline activity at rest. During fictive swimming, their activity decreases and slowly returns to baseline after locomotion termination. Guided by calcium activity, whole-cell current-clamp and voltage-clamp recordings were made to characterize their firing patterns and membrane currents during swimming and resting states. We find that these antimotor neurons have high input resistance and fire tonically at rest. During stimulation-evoked swimming, they receive initial excitation followed by long-lasting tonic inhibition and phasic excitation and inhibition, suggesting inputs from both sensory and motor pathways. Neurobiotin staining of recorded cells reveals that most antimotor neurons possess commissural axons and populationally, they have widespread projections to midbrain, hindbrain and spinal cord regions. Our results elucidate the properties of a cell type potentially involved in behavioral state control in a simple vertebrate.

Poster 38: Coordination of feeding and locomotion behaviors in larval Drosophila: a functional connectomic analysis

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Environmental cues must be translated into coordinated behavioral responses such as feeding and locomotion to ensure survival. In *Drosophila*, a population of neurons in the subesophageal zone (SEZ) expresses the neuropeptide hugin, the homolog of the mammalian neuromedin U (NMU). Like NMU signaling in mammals, activation of hugin neurons suppresses feeding and promotes locomotion. Activation of a subtype of these neurons that projects to neuroendocrine regions of the brain (hugin PC) is sufficient to suppress feeding and promote locomotion, whereas activation of a descending subtype (hugin VNC) increases the contraction frequency of longitudinal muscle M6, which is correlated with crawling. How these hugin interneurons coordinate feeding and locomotor behaviors remains unclear. Analysis of the larval CNS EM connectome revealed that hugin VNC neurons synapse onto interneurons that converge onto motor neurons innervating the lateral transverse (LT) muscles, which contract between peristaltic waves during locomotion. One of these interneurons, A26f, is premotor to these muscles and has been shown to increase locomotor frequency by inhibiting LT muscle activity, consistent with modulation of M6 contraction frequency by hugin VNC neurons. To examine how hugin VNC neurons influence locomotion, we performed dual-color calcium imaging to monitor hugin VNC activity simultaneously alongside glutamatergic motor neurons to record fictive locomotion in an isolated CNS preparation. We find that hugin VNC neurons display oscillatory activity synchronized with the initiation of each fictive peristaltic wave, consistent with activity patterns previously observed in their postsynaptic partner A26f. Connectome analysis further revealed that a population of abdominal sensory neurons makes direct synaptic contacts with hugin VNC neuron and indirect connections to hugin PC neurons via interneurons. Analysis of the whole animal connectome confirmed these inputs as tracheal dendritic (TD) sensory neurons. Using CaMPARI, we show that a subset of TD neurons, as well as both hugin subpopulations, respond to CO_2. In sum, our results identify a sensory-motor circuit in which CO_2 detected by TD neurons engages parallel hugin pathways to coordinate behavior: hugin PC neurons acting through neuroendocrine brain regions and hugin VNC neurons acting through premotor interneurons such as A26f to regulate locomotor output.

Poster 39: The inferior olive transforms upstream sensorimotor errors into cerebellar teaching signals

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Adaptive behavior requires evaluating whether sensory feedback matches expectations derived from motor commands. In cerebellar theories, climbing fibers arising from the inferior olive (IO) convey prediction error signals that instruct learning, yet how these signals are constructed remains unresolved. Using larval zebrafish performing visuomotor behaviors in virtual reality, we combined two-photon calcium imaging with glutamate sensors to measure excitatory input to the IO and climbing fiber output under identical conditions. IO activity scaled with discrepancies between expected and experienced optic flow across open- and closed-loop perturbations. Strikingly, excitatory drive to the IO already contained structured, motor-dependent information consistent with error-like signals. Comparison of input and output revealed selective, frequency-dependent transmission from the olive to the cerebellum. These findings suggest where error representations arise in the olivo-cerebellar pathway and support a model in which climbing fiber teaching signals reflect upstream processing combined with filtering within the IO.

Poster 40: Repetitive trans-spinal magnetic stimulation promotes repair in inflammatory spinal cord injury through sex-dependent immune modulation

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Spinal cord injuries (SCI), whether traumatic or inflammatory in origin, are characterized by neuroinflammation, demyelination, and functional disabilities. Current therapeutic options remain limited, underscoring the urgent need for novel, non-invasive treatment strategies. Repetitive magnetic stimulation (RMS) has recently emerged as a promising neuromodulatory approach; however, its mechanisms of action and therapeutic efficacy in inflammatory contexts remain poorly understood.

In this study, we investigated the effects of RMS applied as repetitive trans-spinal magnetic stimulation (rTSMS) in a mouse model of focal spinal cord demyelination induced by lysophosphatidylcholine (LPC). Our results demonstrate that when rTSMS is initiated one day after LPC injection, it significantly attenuates neuroinflammation, reduces demyelination, and limits fibroglial scar formation. These effects are associated with recovery of locomotor function in both sexes. In contrast, when rTSMS treatment is initiated three days after LPC injection—corresponding to the peak of motor deficits—the therapy confers significant tissue protection and functional improvement exclusively in female mice. To further elucidate the biological mechanisms underlying these sex-dependent effects, we performed RNA sequencing analyses. These analyses revealed distinct patterns of immune modulation: in female mice, rTSMS predominantly regulated adaptive immune pathways, whereas in male mice, it primarily modulated innate immune processes.

Altogether, our findings establish rTSMS as an effective non-invasive therapeutic approach capable of mitigating neuroinflammation and demyelination in inflammatory SCI, with marked sex-dependent outcomes. By identifying distinct immune mechanisms engaged in male and female mice, this study provides novel mechanistic insights into rTSMS action and supports its potential translational application in neuroinflammatory diseases.

Abstracts Accepted but Not Presented

Talk 1: Julia Kaiser (USA) - *Cortico-brainstem output is required for precise and coordinated skilled forelimb movements*

Poster 1: Turgay Akay (Canada) - *Proprioceptive Feedback Orchestrates Homolateral Leg Coupling During Locomotion*

Talk 1: Cortico-brainstem output is required for precise and coordinated skilled forelimb movements

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Skilled movement depends on descending cortical pathways that engage both spinal and brainstem centers. We recently identified a developmentally specified cortico-brainstem pathway arising from a subset of layer 5 neurons that restrict their axons to supraspinal targets from the earliest stages of axon extension. These neurons innervate rostral brainstem nuclei, including midbrain reticular regions and the superior colliculus, and can be prospectively identified by transient Neuropeptide Y (Npy) expression during development. Silencing Npy^+ cortico-brainstem neurons reduces success in the single-pellet reaching task, demonstrating that they are required for skilled forelimb movement. Here, we define how this pathway shapes movement execution. Silencing Npy^+ neurons selectively increased errors during the approach phase of the reach, consistent with impaired forelimb targeting. Kinematic analysis revealed that this deficit did not simply reflect a higher frequency of naturally occurring baseline errors. Instead, silencing induced a reproducible shift in movement structure, giving rise to a distinct reach mode marked by mistargeted trajectories, prolonged outward movements, and unstable paw positioning at the target. This altered movement pattern was observed across reach outcomes, demonstrating that silencing cortico-brainstem pathways alters the structure of motor execution rather than merely increasing failure rates. Together, these findings demonstrate that a developmentally specified cortico-brainstem circuit sculpts the fine kinematic structure of skilled forelimb movements and support a model in which dexterous motor control engages parallel descending cortical pathways, positioning cortico-brainstem output alongside corticospinal projections in skilled movement execution.

See also: **Kaiser, J**., Patel, P., Fedde, S. *et al.* Developmental molecular signatures define de novo cortico-brainstem circuit for skilled forelimb movement. **Nat Commun (2026).** https://doi.org/10.1038/s41467-026-73476-4

Poster 1: Proprioceptive Feedback Orchestrates Homolateral Leg Coupling During Locomotion

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A central goal in motor control is to understand how the nervous system transforms sensory input into spatially accurate motor output. Terrestrial legged locomotion offers an ideal model for investigating this, as it is rhythmic, naturally occurring, and allows for robust, reproducible data collection. A key challenge for all legged animals moving on land is placing their feet precisely on stable ground, a requirement for maintaining balance, especially when navigating uneven terrain or obstacles. In bipedal species, this is largely achieved through visual guidance. In contrast, quadrupeds and other multi-legged animals likely cannot rely solely on visual input to guide their hind limbs, which often fall outside the visual field during movement.

In this study, we asked whether proprioceptive feedback serves as the primary sensory modality for directing hind limb placement during the swing phase in mice. To test this, we combined genetic manipulations with in vivo behavioral analyses. We found that during steady treadmill locomotion, hind limb foot placement at the end of swing is consistent and shows limited dependence on muscle spindle feedback. However, when perturbations trigger a stumbling corrective response, the hind limb begins to track the forelimb's foot placement at the end of stance on a step-by-step basis. This spatial coordination is severely disrupted in the absence of proprioceptive input from muscle spindles.

Using a chemogenetic approach, we further show that forelimb–hind limb coordination relies on supraspinal processing of forelimb proprioceptive signals. Specifically, we identify the cuneate nucleus in the medulla oblongata as a key node in this supraspinal circuit. Notably, our data suggest that the perturbation-dependent switch—from steady-state hind limb placement to step-by-step tracking of the forelimb—is mediated by circuitry within the cuneate nucleus. These findings reveal a proprioceptive mechanism that ensures accurate hind limb placement in response to perturbations and highlight the supraspinal pathways underlying homolateral leg coordination during quadrupedal locomotion.

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