In vivo neuronal dynamics during adaptation to movement perturbations

Sujet proposé par

Stell Brandon / brandon.stell@u-paris.fr

SPPIN
Cerebellar Neurophysiology

M2 Research project title

In vivo neuronal dynamics during adaptation to movement perturbations

Keywords

Sensorimotor integration, optogenetics, in vivo neuropixel, in vivo 2-photon imaging

Description of the project

The ability to learn precise, coordinated motor programs and adapt them to a changing environment is essential for the survival of all animals. A leading theory for how mammalian brains quickly adapt motor programs to perturbations from the environment proposes that the cerebellum compares perceived sensory stimuli (perceived reafference) to a prediction of sensory stimuli (expected reafference) that is based on previous experience (Medina, 2011). Any differences between predicted and perceived reafference are then relayed to the motor cortex so it can adapt future motor programs to the perturbation. This ability to adapt motor commands to the environment is one of the major functions of the brain and there have been recent advances in our understanding of how it is performed (Li and Mrsic-Flogel, 2020). However, gaps remain: Where and how does the cerebellum store the expected reafference that it uses to predict and compare to the perceived reafference? How is activity of the network of cells in the motor cortex affected by differences in perceived and expected reafference that is output by the cerebellum? We propose to use a novel behavior paradigm that we have recently developed (Nguyen and Stell, 2024, bioRxiv) to further investigate, at a cellular level, how cerebellar processing affects motor learning. Understanding the cellular, and network interactions during motor adaptation requires a unique behavioral paradigm that permits simultaneous observation of neuronal and behavioral adaptation to changes between perceived and expected reafference. In a classic experiment in humans, perceived reafference is decoupled from expected reafference using prism goggles that shift the visual field by several degrees while people use ballistic movements (throws) to locate a target in space (Martin et al., 1996a). In healthy subjects, initial failure to locate a target informs future attempts, and subjects adapt motor programs to reliably locate targets extremely quickly (within 10-20 attempts). However, patients with cerebellar deficits fail to adapt motor programs to the new sensory reafference produced by the goggles—presumably because the comparison between the perceived and expected reafference cannot be achieved without the cerebellum. Interestingly, in this paradigm the motor cortex must also be involved in the adaptation because movements are ballistic and subjects do not get feedback that they can use to adjust their performance until after the movement is executed. Therefore, the motor cortex is obliged to use the feedback from previously perturbed commands/trials to modify subsequent commands before they occur. Our recently developed behavioral task in head-fixed mice allows us to observe activity of individual cells in both the cerebellum and recapitulates the essential components of prism goggles experiment in humans: Head-fixed mice use a forelimb to control a joystick that moves a water-port. The predicted and perceived reafference is decoupled by changing the rate at which the water-port moves with respect to the joystick, and mice must use previously perturbed trials to modify future trials. The hypothesis is that the expected reafference associated with a motor command is saved in synaptic weights of synapses onto the cells in the cerebellar cortex that are activated by an efferent copy of the motor command. When the motor command is consistently paired with a novel sensory input, the weights of these synapses change to report the sensory input as a known expectation. The net sum of activity through those synapses is then compared to the net sum of activity in the synapses that relay the perceived reafference into the cerebellum. The cerebellar output then reports any differences between motor (expected reafference) and sensory (perceived reafference) inputs as a modulation of firing rate of the cerebellar nuclei cells that are the output of the cerebellum. Specifically, This project proposes to test these hypothesis using a combination of in vivo electrophysiology, 2-photon imaging, and optogenetics to determine: - Whether a comparison is made in the cerebellum between learned and perceived reafference that is output as a change in spike rates of cerebellar neurons. - How various cell-types in the cerebellum perceive, learn, and store expected reafference associated with a simple motor program.

Methods and techniques

This project will use a combination of in vivo electrophysiology, 2-photon imaging, and optogenetics.

References (at least 3)

Conti, R., Auger, C., 2023. Associative plasticity of granule cell inputs to cerebellar Purkinje cells. https://doi.org/10.1101/2023.03.06.531306 Nguyen, V., Stell, B.M., 2024. Rapid Motor Adaptation via Population-level Modulation of Cerebellar Error Signals. https://doi.org/10.1101/2024.01.03.574031 Tran, V., Miki, T., Marty, A., 2022. Three small vesicular pools in sequence govern synaptic response dynamics during action potential trains. Proc Natl Acad Sci U S A 119, e2114469119. https://doi.org/10.1073/pnas.2114469119

Ecole doctorale de rattachement

ED3C

Aurez-vous la possibilité de présenter l'étudiant à une école doctorale ?

Oui