The role of astrocytes in probabilistic decision-making

Juila Pai*[1], Fatih Sogukpinar[2], Kei Ogasawara[1], Naoki Hiratani[1], Shinung Ching[2], and Ilya Monosov[1]

[1]Washington University School of Medicine in St. Louis – États-Unis
[2]Washington University in Saint Louis – États-Unis

Résumé

In a changing uncertain world, it is crucial for animals to be able to store and flexibly update value representations to guide subsequent behavior. This updating is often called reinforcement learning (RL). RL is thought to depend on basal ganglia circuitry, particularly dopamine-dependent synaptic plasticity in the striatum. Even as the field gains insight into how different neural cell types in striatum contribute to RL computations, the role of astrocytes remains unclear. Astrocytes are known to respond to neurotransmitters and neuromodulators such as glutamate and dopamine, and they have strong intracellular calcium responses that can lead to the release of gliotransmitters capable of modulating synaptic plasticity and behavior. However, whether and how astrocyte function is important for RL is not yet known.

To investigate this, we attenuated astrocyte calcium signaling across different regions of striatum while mice performed a probabilistic bandit task. We programmed in-home cage operant devices (FED3s) with right and left nose poke ports to deliver food pellets with 80% and 20% probabilities, respectively. Side-reward contingencies switched after 20-30 rewarded trials, un-cued to the mouse. Agents performing in this task must continuously update their value representations based on the history of outcomes they receive.
After mice were trained to perform the bandit task, we performed bilateral injections of a viral construct that attenuates astrocyte calcium signaling without inducing astrocyte or neuron death (AAV5-GfaABC1D-mCherry-PMCA; Yu et al, 2018) into striatum. To assess the role of astrocyte function across striatal subregions in RL, we performed injections into ventral striatum (VS, PMCA n=10 mice, control n=9), dorsomedial striatum (DMS, PMCA n=10 mice), and dorsolateral striatum (DLS, PMCA n=12 mice). We found that mice with astrocyte activity attenuated in VS show significantly worse performance post-injection compared to pre-injection, and that this decrease in performance correlates with a decrease in win-stay behavior. In contrast, the DLS, DMS, and control cohorts of mice did not show this effect. To further characterize computations that may underlie this behavioral change, we fit mice's behavior with a Q-learning model. We found that VS astrocyte attenuated mice show significantly noisier decision-making reflected through decreased inverse temperature parameters, but no significant change in learning rates. These results suggest that astrocytes in VS may not directly control value updating per se, but are involved in shaping the effect of learned values on the decision-making process.

*Intervenant