Identifying Prefrontal Cortex Excitatory Neural Correlates to Age-Related Shifts in Decision-Making Strategy Through Fiber Photometry System

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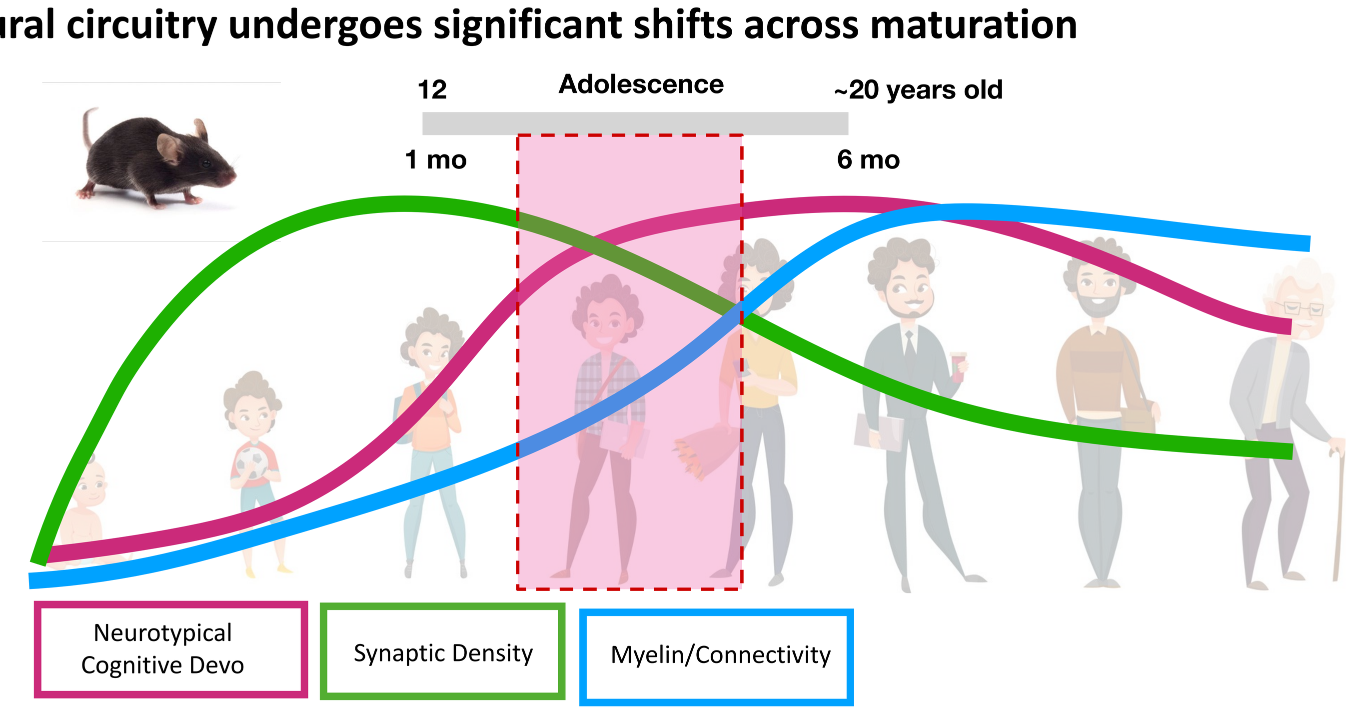
Abstract

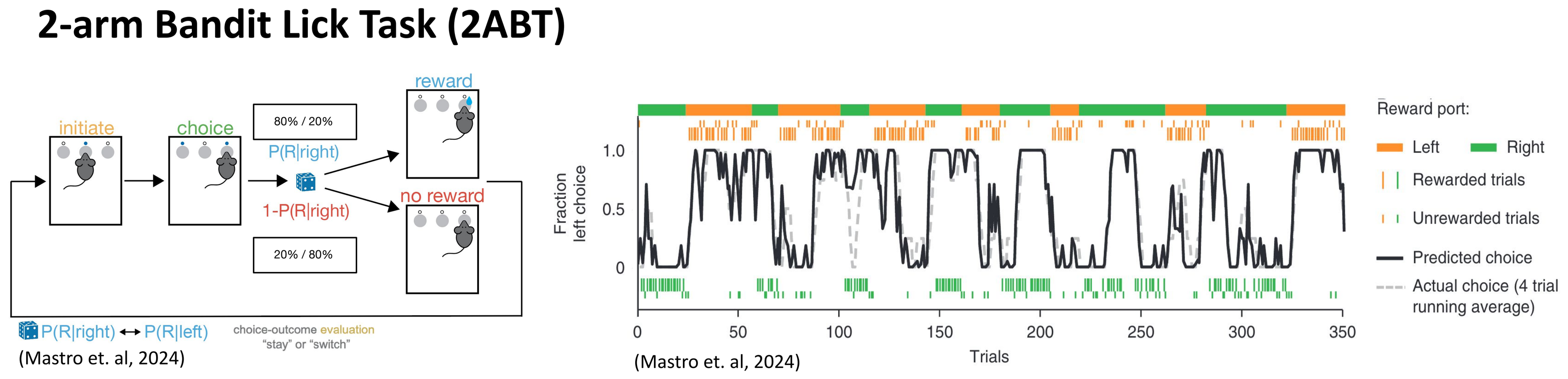
Prefrontal cortical (PFC) circuits are critical for higher cognitive functions, like reward-based decision-making. Moreover, age-related changes in PFC structure parallel age-related changes in decision-making. Our group has also established a marked difference in behavior between young/old amice cohorts on the 2-arm bandit lick task (2ABT). We believe PFC circuit structure may play a role in guiding behavior, and that changes to cognitive function may be tied to changes in the PFC circuit function. Our behavior data showed that 2mo and 4mo old male mice acquired the 2ABT faster than 6mo old mice. During execution, 2mo old mice identified the highly rewarded port faster than 4mo animals following a block transition. 2mo mice also exhibited lower switch probability at block transition than 4mo mice. To simultaneously record the activity of PFC pyramidal neurons of young (P60) and old (P100) mice, we implemented a fiber photometry system utilizing a green calcium sensor. Photometric analysis of the pyramidal neuron activity showed that PFC encodes the trial initiation, action-outcome relationship, and reward history. For example, GCaMP signals decrease in response to reward and increase to unrewarded trials and the magnitude of the change is dependent on the previous outcome history. Subsequent analysis will compare the signaling across the two ages to better understand how observed behavioral changes can be tied to explanatory neural correlates. A further step will look beyond the first 6 months and attempt to understand circuit shifts underlying later-stage cognitive decline, supplemented by high-density multielectrode array Neuropixels which record populations at single-unit resolution.

Neural circuitry undergoes significant shifts across maturation

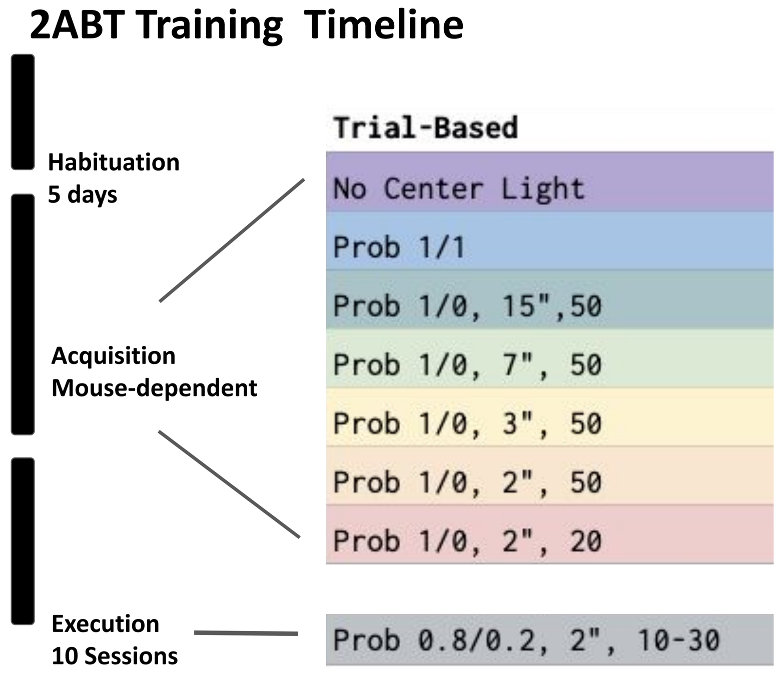


Central Questions
How does 2ABT acquisition and decision-making strategy change across maturation (P60 – P100)? How might the PFC be encoding task variables and guiding behavior differently?

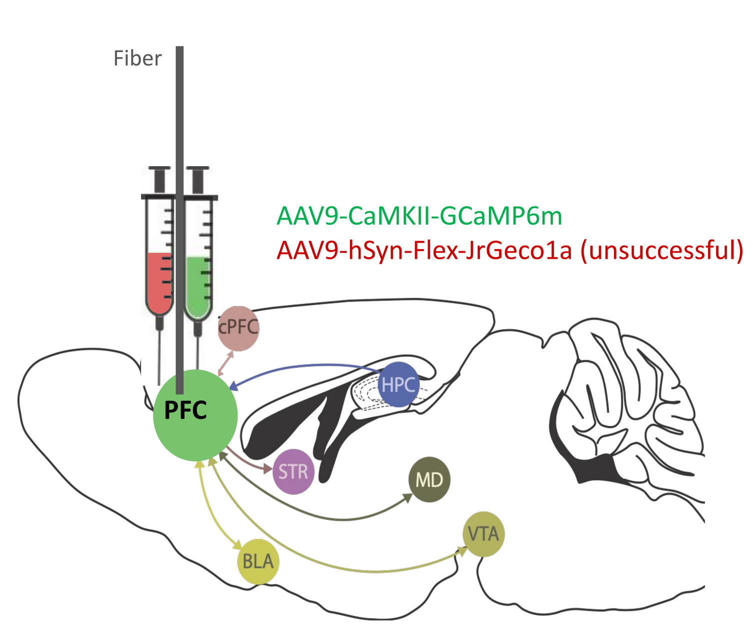
2-arm Bandit Lick Task (2ABT)



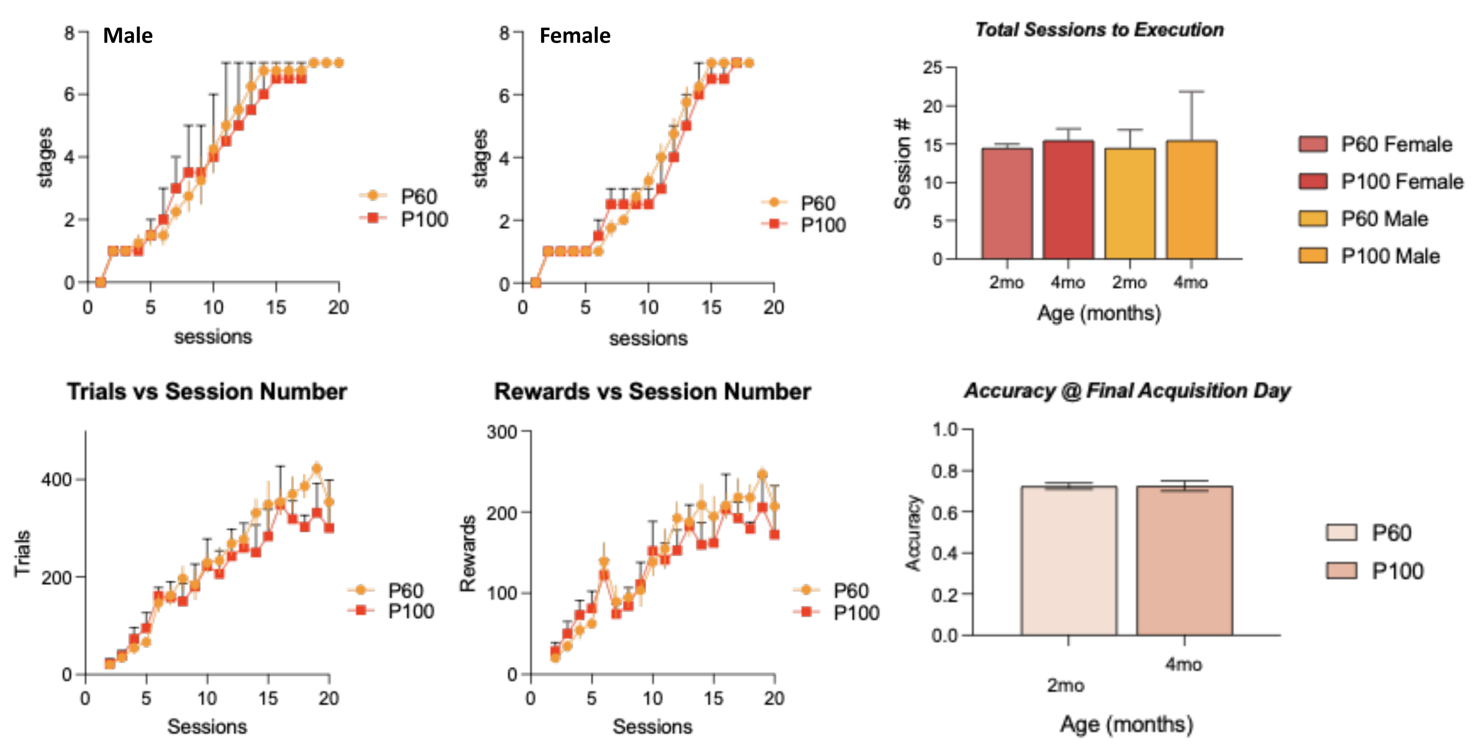
2ABT Training Timeline



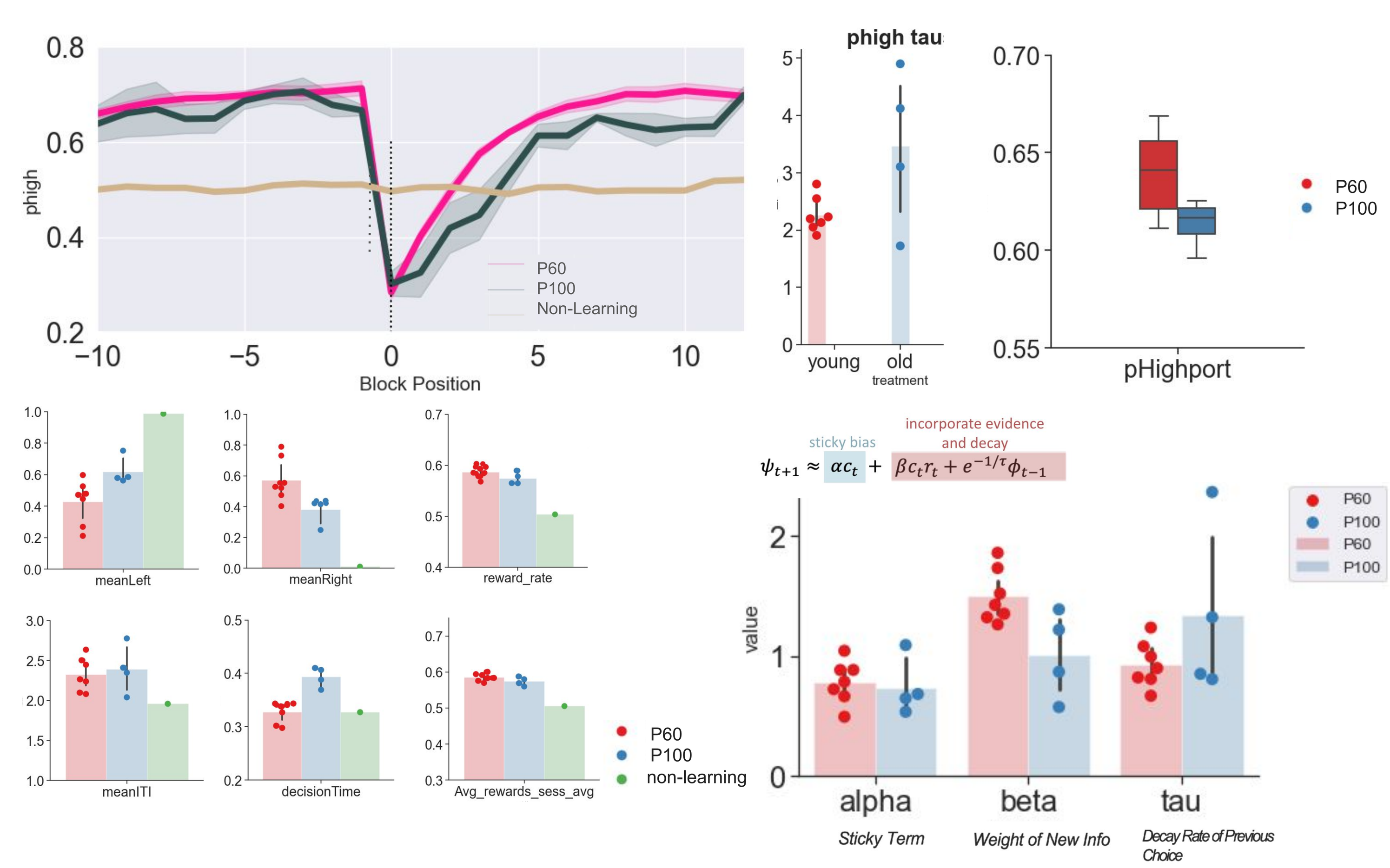
Dual-Color Fiber Photometry in PFC



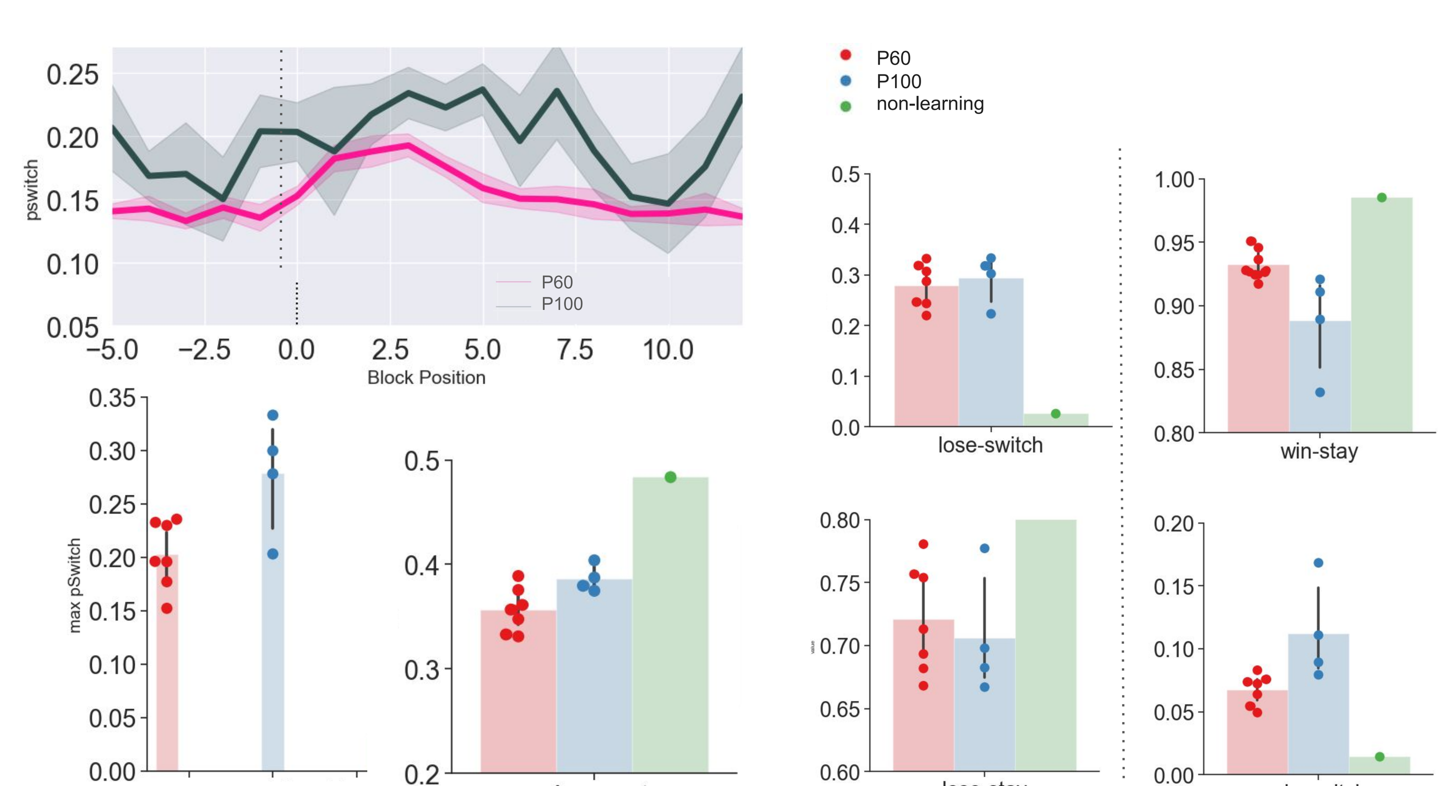
How is acquisition different across maturation (P60–P100)?



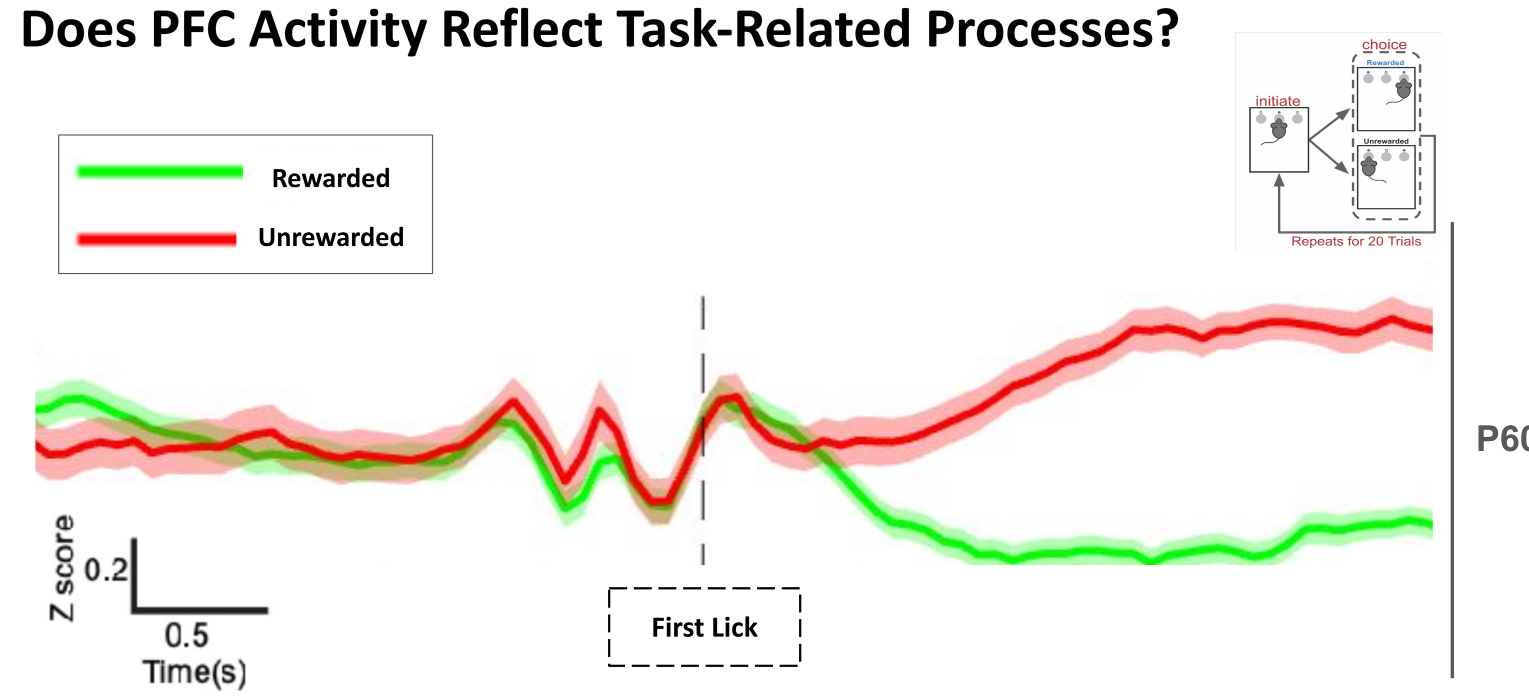
Under probabilistic reward conditions, are P60 vs P100 animals playing the game differently?



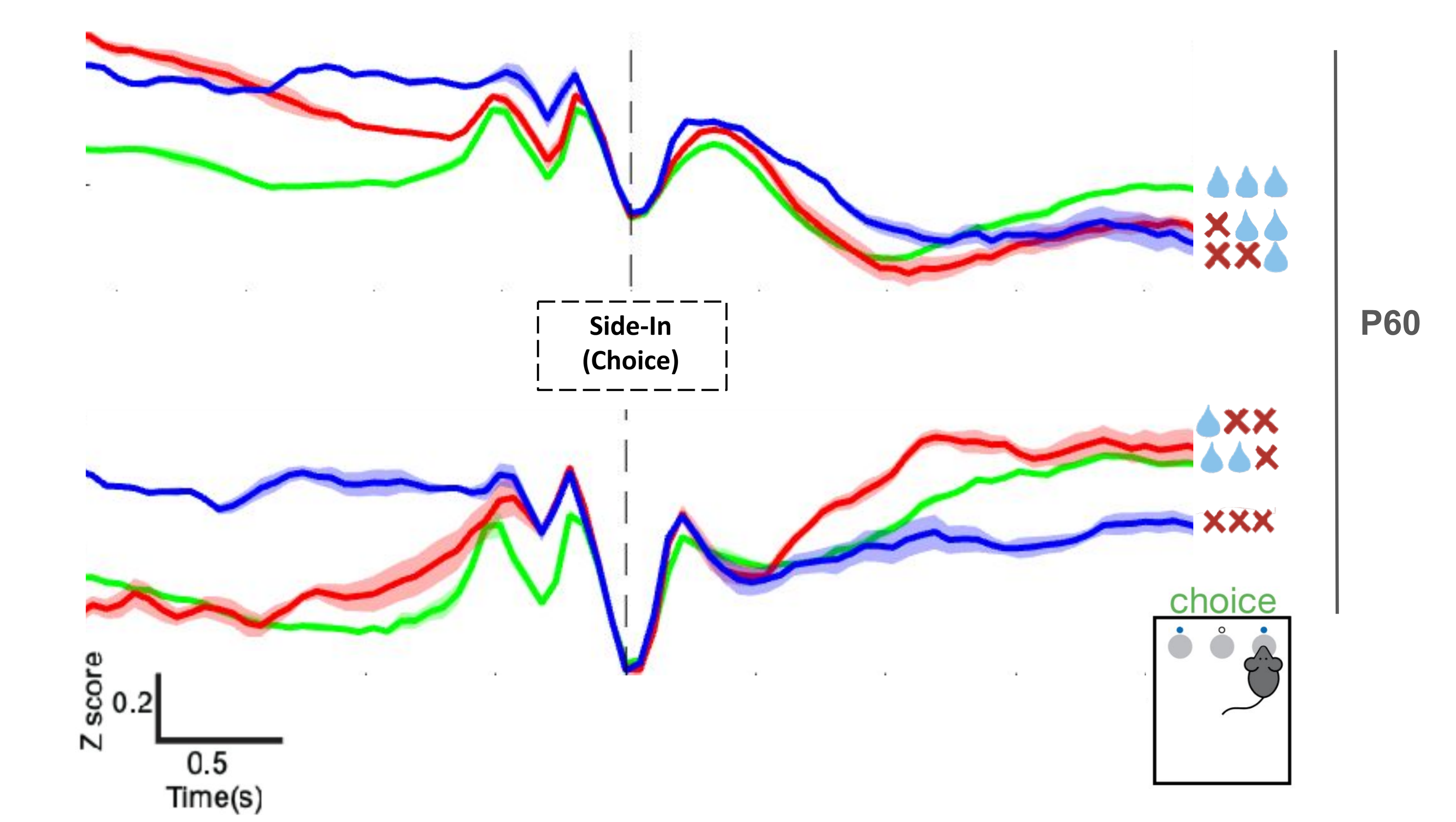
Is there an switch between “exploitative”/”explorative” strategy across maturation?



Does PFC Activity Reflect Task-Related Processes?



How does the PFC encode reward outcome/history?



Conclusion & Future Directions

Our results indicate similar acquisition capacities but a shift in behavior at execution across maturation (P60-P100) – decreased weight of new information, increased decay rate of previous choice, and modified switch strategy. Photometry signaling also displays PFC reward encoding. Subsequent analysis will compare signaling across the two ages to better understand how observed behavioral changes can be tied to explanatory neural correlates. A further step will look beyond the first 6 months and attempt to understand circuit shifts underlying later-stage cognitive decline and/or neural correlates of neuropsychiatric conditions, utilizing Neuropixels which provide single-unit resolution for population photometric observations.

Acknowledgements

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