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Catecholamine Signaling in CA1 Correlates with Novelty, Movement, and Sleep State

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Key Words: CA1, Locus Coeruleus, Fiber photometry, Catecholamines, Novelty

BACKGROUND

The hippocampus is crucial in memory processing, and has a principal role in storing declarative and spatial memory. Norepinephrine (NE) and dopamine (DA) signaling in the hippocampus are important for normal learning and memory. When these catecholamines are blocked, memory deficits occur and synaptic plasticity is thus inhibited. It is critical to understand the underlying principles of how the brain changes with learning in order to develop treatments to improve learning and reverse memory deficits.

Previous micro-dialysis studies have found an increase in hippocampal catecholamines in response to novel environmental exposure or exercise. However, since animals move in response to contextual novelty, it is unknown whether the changes in dopamine and norepinephrine are due to novelty or other changes in behavior or arousal. Outside of the hippocampus, arousal, novelty detection, reward, and sleep state are all related to catecholamine signaling. In this study, we investigated how catecholamine signaling in the hippocampus relates to novelty and movement. We also investigated the role of catecholamines on reward and sleep state.

HYPOTHESIS

When mice initiate exploratory movement, we expect a strong increase in DA/NE following initial object presentation that decreases over time. If the response is related to novelty and not movement, we expect a decrease in catecholamine release. If an increase in DA/NE following initial object presentation that decreases over time.

OBJECTIVES AND RATIONALE

To de-confound signals caused by novelty and exploratory movement
To understand the roles of dopamine and norepinephrine in reward prediction
Moreover, little is known about the conditions under which dopamine is converted to norepinephrine, nor is it known why there are two neuromodulators in the same synapse. This study aims to understand the relationship, if any, between DA and NE under varied conditions (novelty, movement, sleep, reward).

MATERIALS AND METHODS

AAV Injection + GRAB DA/NE Sensors

Fiber photometry to measure DA/NE levels

RESULTS

Figure 1: AAV injection site, green represents the fluorophore

Image 6: AAV injection site, green represents the fluorophore

Figure 2: Experimental setup. Light at an excitation wavelength is input and the resulting emissions are measured with a spectrometer. The resulting and experimental waveforms are separated through signal processing.

Figure 3: Increase in catecholamines when mice are transferred from their homecage to the track. No significant difference between regular track and track with novel object.

Figure 4: Elevated levels of catecholamines on the track that deconfound between novelty and movement.

Figure 5: Velocity of the mouse strongly correlates with catecholamine release

Figure 6: Signal centered around the initiation of object sampling. Over the sampling window, the signal decays and catecholamine levels decrease

Figure 7: Norepinephrine decreases after reward is administered, likely due to animal stopping to drink. Dopamine signals are more varied after single events.

Figure 8: Dopamine changes at transition state. High dopamine response at wake state and low response during REM.

REFERENCES


FUTURE OBJECTIVES

1. Collecting data with more mice to understand the release of DA/NE after reward administration.
2. To determine how much of the neural activity from the novel objects task is due secondary to movement with the mice.
3. To explore parameters (novelty, reward, movement) through a statistical model.
   a. Regress out the movement-related DA/NE signal.
   b. Find movement related to novelty.

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CONCLUSIONS

Dopamine and norepinephrine increase when transferred and when placed in new environment (in this case, the linear track). In their homecage, catecholamine levels stay consistently lower.

Movement is associated with an increase in catecholamines.

Novelty responses are associated with the introduction of objects but not the sampling of objects.

Catecholamine levels when reward is administered is still unclear, though norepinephrine shows a decrease.

When double reward is randomly administered, reward prediction error experiments are not reflected in DA, and if present only weakly evident in NE.