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Research Award Brief

On the Willingness to Invest Time in the Pursuit of a Goal (2017-2019)

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Research Question: How is learning motivated? The facility by which an agent learns from its environment is rooted in its willingness to pursue a goal, despite the cost in time and effort needed for its attainment. In weighing the presumptive costs and benefits, how ought this drive to pursue a goal be calculated by the brain in order to motivate the most beneficial behaviors, what are the neurobiological origins of this drive, and how does it go awry in cognitive disorders?

Interdisciplinary Approach: We address these questions by uniting expertise of two labs, combining theoretical neuroscience, imaging, and behavioral electrophysiology with human psychophysics as examined in patient populations. We develop a mathematical theory which solves for how motivated one should be to invest time to attain a goal, assess its merit in two behavioral tasks while examining the serotonergic system, and connect these insights to behavior in healthy humans and in humans whose serotonergic system is dysfunctional (as in Obsessive Compulsive Disorder, OCD, patients).

Potential Implications of Research: We propose a novel and rigorous formulation of serotonin that explains its contribution to patience for delayed rewards and sensitivity to expected reward, test this theory, and apply these insights to human disorder (OCD). Translating new neurophysiological insights regarding the role of serotonin could be leveraged to treat cognitive disorders affecting the serotonergic system, such as in OCD, where dysfunction of the serotoninergic system is implicated as a root cause.

Though the most common psychopharmacological target, the precise pathophysiology of disorders affecting the neuromodulator serotonin remains elusive. A complete explanation of serotonin's function awaits a computationally rigorous theory uniting serotonin's natural pattern of activity to its known effect on behavior. We have developed such a theory and designed several behavioral assays specifically suited to testing it.

By identifying the calculations that would enable an animal to achieve maximum total reward over time, we hypothesize that **serotonin signals the value of continuing to invest time in pursuit of a reward**. These calculations provide the first complete normative explanation of temporal discounting observations. They also highlight a critical new variable: background reward rate. When the background reward rate is high, the opportunity cost of time-expensive pursuits is higher, so that delayed rewards become, relatively, worth less for the time they require.

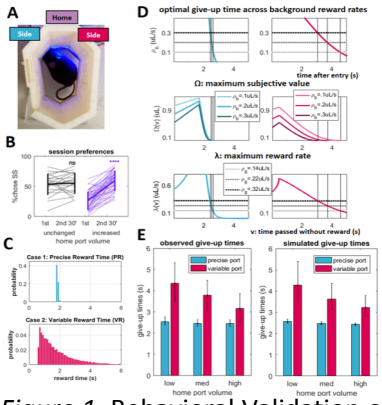

Figure 1. Behavioral Validation of Theory
A) behavioral chamber. B) Choice task. C) Give-up time task: reward time distributions. D) *Top*: Give-up times maximizing reward. *Middle*: The maximum subjective value. *Bottom*: The maximum reward rate of the port (λ) E) *Left*: observed give-up times. *Right*: simulated give-up times.

To test our hypothesis, we will record single-unit and optically image serotonergic neuronal activity as animals decide how to invest time across reward options differing in their known temporal distributions. We will also test if optogenetically augmenting serotonergic activity perturbs temporal investment in the particular, identifiable manner specified by theory. A rigorous theoretical understanding of the natural function of serotonin could improve understanding of psychiatric conditions affected by serotonin dysfunction and lead to more effective therapies. To that end, we will examine healthy and OCD patient populations in human versions of the tasks developed to assess how the willingness to invest time in the pursuit of a reward is evaluated and acted upon.

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