Green Means Go: The Role of Norepinephrine in Attention and Learning

Households are full of distractions under normal circumstances, but now that much of our workforce is working from home and students are attending school virtually, distractions are at an all-time high. How do we control our attention and how can we help those who have trouble doing so?

Attention is the ability to hold on to information from our environment and select the important components for response. Attention-deficit/hyperactivity disorder (ADHD) is one of the most common psychiatric conditions affecting almost 11% of children ages five to seventeen.[1] While treatments exist for disorders of attention, many are coupled with side effects on mood, sleep and appetite. To develop effective interventions, we need to better understand the connection between molecular mechanisms in the brain and behavioral impairments in attention and learning. Assistant professor at the UC Davis Center for Neuroscience, Timothy Hanks, Ph.D. received one of five pilot awards for a collaborative study examining this connection titled, "The role of norepinephrine-induced neuronal plasticity in attention and learning."

Stoplights to test attention

ADHD is defined by patterns of inattention, hyperactivity and impulsivity that interfere with one's functioning. The Hanks lab uses a mouse model and a task that simulates situations that demand attention. The researchers measure the animal's ability to pay attention, not respond too quickly and not get distracted, analogs for the most common symptoms of ADHD. The task uses a bank of lights similar to what you might experience at a stoplight. Each light corresponds to a particular action, for example, you could be presented with a left green arrow, a red light or a solid green light, each of which precipitates a particular response that requires attention and timing. With an animal model, the researchers can adjust the signals, measure behavior and response, and perform trial and error testing to understand the mechanisms underlying the animal's attention.

Recipe for attention

Our brains adapt and change in response to the environment. Chemical messengers, called neurotransmitters, affect the brain's function in response to behavioral stimuli. Norepinephrine is important for arousal, attention, and learning. The most common ADHD medications target either norepinephrine or dopamine concentrations in the brain to improve attention. However, little is known about the specific interactions that lead these medications to be more or less effective across individuals.

Hanks uses an analogy of cooking to describe the goal of his project, "Imagine you can only add or remove salt to improve your cooking and all meals must receive the same treatment. Some meals

"This pilot grant allows us to broaden the scope of our research and ask questions that are more translational and develop principled treatments."

-Timothy Hanks, Ph.D.

might be improved and others might be ruined. In extreme cases the additional salt to improve one meal is worth its effect on the others; but what if we could be targeted about which meals get salt and how much?"

The research team will use cutting edge techniques to measure and manipulate neurotransmitter signaling in the brain. One of these techniques involves using new molecular sensors developed at UC Davis by associate professor, Lin Tian, Ph.D. to directly measure neurotransmitter release. When animals are presented with attentionally demanding tasks the researchers have the tools to measure the brain's response. "These tools offer unprecedented access to brain signals that occur during behavior and are important for attention. These innovative techniques will provide insight into the specific mechanisms involved in attention," said Hanks.

Targeted Interventions

The research team aims to develop targeted interventions that impact the specific mechanism and improve the recipe for attention without impacting the other recipes for mood, sleep, or appetite in unsatisfying ways. The team is looking at how attention is regulated and hypothesize that norepinephrine is a major player in the control of attention through a specific molecular pathway involving calcium channels. By understanding the signaling pathways involved in attention-dependent learned behavior this pilot has the potential to impact the development of novel treatments for attention and learning deficits.

The collaborative nature of this grant brings together expertise in systems, behavior and computational neuroscience from Dr. Hanks and expertise in molecular and cellular neural plasticity from Dr. Johannes Hell. The pilot funding will support the pipeline of scientists committed to better understanding the brain and behavior including Kyle Ireton, a postdoctoral student in Dr. Hanks' lab.

1. HUS, 2018 https://www.cdc.gov/nchs/fastats/adhd.htm

Behavioral Health Center of Excellence at UC Davis

UC Davis launched the Behavioral Health Center of Excellence in October 2014 to advance mental health research and policy with initial funding from the Mental Health Services Act. The Innovate series highlights the Center's research pilot award program.

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