Project Title: Neural Circuits Implicated in Dysautonomia
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Abstract:
Dysregulated autonomic function, or "dysautonomia", is prevalent in many neuropsychiatric and neurodevelopmental disorders, including anxiety disorders and autism spectrum disorder. Dysautonomia may arise from a problem in how the central nervous system regulates the adrenal medulla. However, the neural circuits that control the adrenal medulla's sympathetic output are not fully defined. Filling this fundamental gap in knowledge is crucial to understanding how the circuit may go awry in neuropsychiatric and neurodevelopmental disorders with prominent dysautonomia

We propose to fill this gap by defining the neural basis of sympathetic responses. The student's focus will be defining the limbic sites that control these autonomic responses. Through an 8-week immersion to translational neuroscience, the fellow will define the regions of the amygdala and hippocampus that regulate the non-human primate adrenal medulla. The student will develop advanced skills in neuroanatomy to reconstruct these limbic systems that send multi-synaptic projections to influence the sympathetic output of the adrenal medulla. Specifically, they will identify cells labeled with a trans-neuronal tracer (rabies virus). Then, they will reconstruct these outputs to reveal the limbic systems that influence the sympathetic nervous system.

The results from these experiments have the potential to identify specific regions of the limbic system that contribute to, and could be therapeutic targets for, autonomic dysfunction in neuropsychiatric and neurodevelopmental conditions.

Mentorship Plan:
The fellow will meet formally with Dr. Seese twice weekly during the fellowship period:
1. During the first 1-hour weekly meeting, the student will critically appraise an assigned journal article 1:1 with Dr. Seese. The training has three over-arching goals. First, to develop skills in how to critically review both pre-clinical and clinical literature. Second, to develop a foundation of knowledge for the field's current biology. Third, to determine how their results fit within the field's gaps in knowledge to answer clinically important questions.
2. During the second 1-hour weekly meeting, the fellow and Dr. Seese will review data obtained over the prior week. We will discuss how that fits in with other preliminary data from the lab. We will discuss the advantages and limitations of the methodology being used.
3. The student will have informal contact with Dr. Seese on nearly a daily basis during the fellowship period.

Resources Available:
1. The fellow will have unlimited access to all resources needed to complete the proposed analyses. This includes a website to plot immunolabel neurons and a program to reconstruct neural systems. The student will require a personal computer and reliable internet connection.
2. Using a secure website, the student will plot neurons labeled with a viral trans-neuronal tracer from scanned brain sections. The fellow will then define sites of labeled neurons using in-house reconstruction software. These analyses will allow the student to create "maps" of deep cerebellar neurons and cerebellar cortex Purkinje cells that influence sympathetic output. These analyses can be done virtually on the student's personal computer.