November 15, 2022

Michelle Jones-London, Ph.D.

National Institute of Neurological Disorders and Stroke

Re: Letter of Intent for F99/K00 “*Neural and Behavioral Representations of Social Ambiguity Among Adolescents and Adults*”

Dear Dr. Jones-London,

I am writing to let you know that I plan to submit an F99/K00 application for RFA-NS-21-012, “*Neural and Behavioral Representations of Social Ambiguity Among Adolescents and Adults*.” The research team will consist of myself, Dr. Chelsea Helion (Primary Sponsor), and Dr. Jason Chein (co-Sponsor) and the research will be conducted at Temple University.

As an aspiring developmental neuroscientist from a disadvantaged background matching the outlined NIH criteria, the NIH Blueprint Diversity Specialized Predoctoral to Postdoctoral Advancement in Neuroscience Award is a unique opportunity to ensure that I excel as a future independent academic researcher. It will certify that I have the funding necessary to complete the course of formalized training that I have outlined in the grant and allow me to pursue a programmatic line of impactful research relevant to vulnerable developmental populations.

Although ambiguity (i.e., unknown probabilities for unclear outcomes) can be an aversive hallmark of a social world, we know very little about how individuals form judgments of certainty in response to social situations and regarding social outcomes. The increased valuation and prioritization of social others during adolescence places adolescents in a precarious position, as the presence of ambiguous social stressors during this period predicts long-term susceptibility to and severity of anxiety and depression. This research is difficult to square with the extant literature suggesting that adolescents, unlike adults, do not demonstrate ambiguity aversion, but little attention has been paid towards the social domain in this regard. To better understand the relationship among development, ambiguity, and long-term psychopathologies, we must understand how differences in how adults and adolescents attend to information, mechanistically process that information, and form judgements of that information over time.

The proposed research uses a novel naturalistic fMRI paradigm wherein participants watch a video (e.g., crime drama) while continuously rating how certain they are of a given outcome (e.g., a character is innocent). In combination with eye-tracking and free-recall, we can identify neural and behavioral correlates of ambiguity as well as how attention and stimuli features inform certainty judgements. Furthermore, by using the same stimulus but changing the target outcome (e.g., frame luminance), we can begin to parse apart differences in the formation of social and non-social uncertainty. I have used this paradigm successfully with adult participants to identify neural regions activating during social and non-social uncertainty judgment formation, including orbitofrontal cortex, inferior frontal gyrus, temporal pole, and the superior frontal gyrus. The goal of the proposed research would be to leverage this approach to identify developmental differences in the representation and formation of uncertainty judgements.

As such, **my dissertation research project (F99 Phase) will aim to explore the formation of outcome-based social uncertainty judgements across normative adolescent development.** By applying intersubject representational similarity analytic approaches, I can create multimodal computational models to explore how these different components of uncertainty contribute to its global representation and how those representations differ as individual mature in this early lifespan transition. Developing expertise in social affective developmental neuroscience literature and computational methods represent a primary learning aim of my proposal which will give me the skills I need to begin a career as an independent developmental neuroscience researcher.

**During my postdoctoral studies, I aim to compare the efficacy of and mechanisms behind different regulatory strategies to manage uncertainty.** If uncertainty is associated with negative long-term health outcomes, mitigating aversive responses to uncertainty should be of the utmost concern to researchers. However, recent meta-analyses highlight that adolescents demonstrate observable performance deficits using many of the most studied self-regulation strategies (e.g., reappraisal). An alternative perspective-based self-regulation strategy has been tested within our lab among adults and has demonstrated efficacy in moderating certainty judgments behaviorally. Because role-play develops as early as 3 years old, can be naturally engaging, and relies on neural circuitry which is unique from reappraisal and may undergo relatively less developmental maturation, perspective-based self-regulatory approaches may represent a promising avenue to manage the aversiveness of uncertainty early in life.

Thank you for your time and I look forward to submitting my proposal for your consideration.

All the best,

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