Spring 4-25-2024

Neural Activation Patterns during Socially Transmitted Aggression

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Title: Neural activation patterns during socially transmitted aggression
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ABSTRACT

Children who experience abuse or witness it are at an elevated risk of becoming either victims themselves or engaging in violent behavior later in life, possibly due to the observed behavior of the abuser or the abused. However, socially transmitted aggression remains understudied due to the absence of a suitable behavioral paradigm. This study addresses this gap by introducing a novel social transmission paradigm combined with fiber photometry to explore the brain regions implicated in socially transmitted aggression in mice, given the conservation of their circuity and impact on aggressive behavior. This study addresses this gap by introducing a novel social transmission paradigm combined with fiber photometry to explore the brain regions implicated in socially transmitted aggression in mice.

It was imperative to acquire an in-depth comprehension of aggression models utilized in preceding investigations. A thorough examination of multiple publications in the Morris Library database focusing on socially transmitted aggression and early-life stress, specifically employing fiber photometry techniques, was conducted. This literature review facilitated the formulation of a robust model to attain the anticipated outcomes. Notably, the database encompassed articles previously disseminated by the Nordman Lab, serving as pivotal resources for elucidating social transmission models utilized in their prior research. This comprehension was instrumental in devising an animal model capable of representing the nuances of human experiences after instances of aggression and abuse. Through utilization of the resources offered by the Morris Library database, we adeptly devised a rodent model to execute the project with optimal efficiency and effectiveness.

KEYWORDS:

- Abuse
- Social transmission
- Aggression
- Mouse model
- Neural mechanisms
- Medial amygdala
- Fiber photometry
- Witness behavior
- Calcium signaling
- Therapeutic implications

PROJECT DESCRIPTION

Research Statement

The perpetuation of abuse is a significant issue for its victims and society as a whole. Abused children are at a higher risk of either further victimization or of perpetuating violence later in life. Previous research has shown that children who have experienced abuse or witnessed abuse are at a higher risk of further victimization or perpetuating violence in the future (Stiles, 2002). One potential explanation for this is that these children may model their behavior on either the abuser or the abused (Laplanche and Pontalis, 1967). However, directly testing this hypothesis is challenging due to logistical and ethical constraints.

Like humans, mice are social animals that to do much of their learning through social transmission. For example, mice can infer fear from watching another mouse's response to a fear-inducing stimulus rather than needing to experience the stimulus directly (Atkinson et al., 2020). Mice are also an ideal animal model when studying human aggression as their neurocircuitry and its effect on aggressive behavior is largely conserved (Nelson and Trainor, 2007). However, socially transmitted aggression has not been studied due to a lack of a suitable behavioral paradigm.

In this study, we will use our newly developed new social transmission paradigm combined with fiber photometry, described below, to investigate the brain regions involved in socially transmitted aggression in mice. It is our hope that once the neural mechanisms of socially transmitted aggression are characterized, newer and better therapies can be developed to treat extreme anger and violence.

Background

To identify brain regions involved, we analyzed the medial amygdala (MeA) using cFos immunohistochemistry, indicating a trend towards increased aggression. To assess real time changes in the activity of MeA neurons in witnesses to demonstrator attack behavior, we will use fiber photometry. Fiber photometry is a live imaging technique

that captures the population activity of specific cell types in a defined region of the brain using fluorescent reporters such as the calcium indicator GCaMP6f (Dana et al., 2019). This involves using a calcium indicator virus in the MeA and implanting optical fibers for live recordings. These experiments aim to further elucidate the role of the MeA and other brain areas in socially transmitted aggression.

Methodology/Approach

Three-week-old mice will be group-housed for three weeks before undergoing surgery. The mice will be anesthetized and injected with an adeno-associated virus (AAV) encoding the calcium indicator GCaMP6f or a GFP control virus into the medial amygdala (MeA). This procedure, using a stereotaxic frame, ensures precise delivery of 300 µl of the virus. After the injections, 200 µm diameter optical fibers will be implanted into the MeA for site-specific recordings during behavioral testing. Following a two-week recovery period, the mice will be acclimated to the novel arena for two more weeks. On the test day, patch cords will be attached to the optical fibers, connected to a fiber photometry system that detects the green light emitted by GCaMP or GFP. Recordings will be made during behavior assessments. Finally, histology will confirm the accuracy of viral targeting and fiber implantation.

Statistical analysis

Changes in calcium signaling will be calculated from ΔF/F that is normalized to the isosbestic point (Kim et al., 2016). Photometry signals will then be aligned to attacks and averaged using an established protocol (Hashikawa et al., 2017). One-way ANOVAs will be used to assess for significant group differences between each time point during the recording session. Paired t-tests will be used to assess for changes in fluorescence from baseline to each time point during and immediately after an attack. Two-way ANOVAs will also be used to assess for group differences in calcium signaling between the various groups.

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