Background

Cognitive decline is one the many effects caused by aging. This can be shown in rat models via delayed non-match-to-sample performance (DNMS) tests. [1] Previous studies show that alterations of myelin function due to old age are important contributors to this decline. [2] Myelin is a sheathe that covers axons, providing electrical insulation that speeds up the propagation of action potentials, and thus neuronal signals. Disruption of myelin alters the electrophysiology of axons, which has evident detrimental effects. In the central nervous system (CNS), myelination is done by cells called oligodendrocytes, which differentiate from oligodendrocyte precursor cells (OPCs). Recent studies have shown that myelin alterations due to old age are caused by a disruption of OPCs due to G-protein receptor Gpr17. [3] This receptor is overexpressed in aged OPCs and stops them from differentiating and thus impedes remyelination. A region where lesions and disruption of myelin can lead to cognitive disfunction is the medial prefrontal cortex (mPFC). [4] [5] In studies done on the motor cortex, it was shown that optogenetically-induced oligodendrogenesis leads to increased myelination and increased motor performance. [6]

Aim

Determine if optogentically-induced oligodendrogenesis leads to improved cognitive performance in aging mice.

Research Plan

- The mouse model to be used in this study is the Senescence Accelerated Mouse-Prone 8 (SAM-P/8). This strain exhibits traits that correspond with aging, such as memory difficulties. [7]
- The experimental group will be injected with AAV-ChR2 in the mPFC and allowed to recover for 2 weeks. The control group will consist of mice without optogenetic stimulation.
- After recovery, the experimental group will be sedated, and optical fibers will be placed to stimulate the mPFC. They will be left to recover from the surgery for 1 week
- The experimental group will be stimulated with 470nm blue light for 30s intervals every 2 minutes over a 30-minute period, as done in the study by Gibson, et al. [6] The mice will rest for an hour and the process will be repeated 2 times. The mice will then rest for the day.
- The following day, both groups will be subjected to DNMS tests.
- After comparing results from both groups, the expected result is that the experimental group will demonstrate better cognitive performance in contrast to the control group.

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