INTRODUCTION

Astrocytes are a type of glial cell within the central nervous system that have a pivotal role in maintaining the blood brain barrier, helping metabolic processes and supporting synaptic transmission. Previous research has indicated a role for astrocytes in memory. We employed a chemogenetic technique (Designer Receptors Exclusively Activated by Designer Drugs, or DREADDs) to specifically increase intracellular calcium level and activate hippocampal astrocytes in Long Evans rats during spatial working memory (SWM) using a delayed spontaneous alternation task. Our hypothesis is that activating astrocytes will increase their supportive functions, hence improve working memory (measured by percent spontaneous alternation). Previous research has used clozapine-N-oxide (CNO) as an agonist for the DREADDs receptor, however this has been shown to metabolize to clozapine, which can have effects on a variety of receptors. In the current experiment we use Compound 21 (C21) which was purported to have less effects on endogenous receptors as it does not metabolize to clozapine, however whether C21 itself has effects similar to clozapine has been debated.

METHODOLOGY

RESULTS

DISCUSSION & FUTURE DIRECTIONS

- From the current data, it is likely that C21 alone is having effects on behavior:
  - We found significant increase in the total amount of arm choices in the females with C21.
  - There is an overall trend for a decrease in spontaneous alternation with C21.

- In the future we plan to increase our sample sizes in the hopes that this will clarify some of the effects.

- We will assess the extent of the viral expression. If there is a relationship between the number of astrocytes expressing the DREADDs virus and behavioral outcomes, this may inform how we can modify the study design to improve the effectiveness of the DREADDs activation. Specifically, if increases in viral expression correlate with behavioral effects it may allow us use larger viral injections and reduce the dose of C21. Using CNO is also possible, however it is unclear that the side effects of CNO would be an improvement.

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