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CAN MAGIC MUSHROOMS REMOVE INHERITED TRAUMA?

Caleb Edwards

Bio 488, Fall 2021, Longwood University

Background

- Rats trained to be afraid of a particular smell (acetophenone or propanol) can pass on this fear to their grandchildren, even when the grandchildren were not trained to be afraid (Dias and Ressler 2014)
- The active ingredient in magic mushrooms, psilocybin, has been demonstrated to have a beneficial effect on the treatment of depression, substance abuse disorders, and post-traumatic stress disorder (Vollenweider and Preller 2020)
- Psilocybin can make mice trained to be afraid of a stimulus unlearn this fear response faster than a mouse not exposed to psilocybin (Catlow et al 2013)
- Psilocybin works in part by promoting the connection between neurons and the growth of neurons in the hippocampus (Catlow et al 2013)
- The hippocampus plays a role in emotional memory, approach-avoidance conflict, and memory formation, among other processes. Reduced activity in the hippocampus leads to a worsening of post-traumatic stress disorder symptoms (Astur et al 2006)
- Psilocybin also works to effectively reset parts of the default mode network responsible for communication throughout the brain (Grandien et al 2020)
- Psilocybin-assisted psychotherapy has been granted emergency breakthrough status by the FDA (Hardy 2019)

Hypothesis:

- We propose that the offspring of mice trained to have a fear response will unlearn this fear response faster when exposed to a certain level of psilocybin than offspring of trained mice that are not exposed to psilocybin.
- Mice with a greater hippocampus volume will undergo fear extinction sooner than mice with a smaller volume
- Offspring of mice given psilocybin will have a larger hippocampus with more connections than offspring of mice not given psilocybin

Potential Results:

- Mice who were exposed to psilocybin while gestating will have a faster fear extinction response than mice that were not exposed to psilocybin or were not exposed over as many generations
- Offspring of mice who were exposed to psilocybin will have a greater hippocampus volume and the number of connections will be greater
- This increase of hippocampus activity will increase with each subsequent generation of psilocybin exposure, up to a certain point
- If there is a noticeable effect on the fear extinction response, then further research could investigate if the extinct trauma remains in generations after the proposed breeding groups
- Further research could also investigate if there are other changes to hippocampus function, such as whether or not psilocybin could influence mental mapping done by the hippocampus
- Psilocybin assisted therapy could have downstream benefits in preventing trauma even in an individual who was not exposed, provided their parents were
- The volume and number of connections in the hippocampus could be compared between generations and between the control and experimental groups
- Gene expression in these brain regions could also be compared between groups

Procedure

- This experiment has two main experimental groups: one lineage exposed to psilocybin without trauma during generation 1 (G1c), and one lineage exposed to both psilocybin and trauma during G1 (G1a/b)
- G1c will be exposed to psilocybin without trauma as a control group to determine if psilocybin results in hippocampal growth and development over generations if no trauma is involved
- G1a/b will be trained to have a fear response to the smell of acetophenone through an electric shock when they are exposed to acetophenone after they have bred but before gestation is over. This process will produce the “b” groups
- The fear response will be measured in the number of trials it takes for each mouse to undergo extinction of the learned fear response
- Extinction of the fear response to acetophenone will then take place without the use of psilocybin before gestation of “a” groups
- A fear response to propanol will then be trained and will undergo extinction during psilocybin exposure while the next “a” generations are gestating
- Subsequent generations descended from G1a/b will then be split into two groups: one litter born before extinction of the fear response through exposure to psilocybin and another litter born after their parent was exposed to psilocybin and extinction of the fear response
- This process will continue for at least four generations (Figure 1)
- This breeding arrangement effectively allows for many smaller experimental groups as well as comparisons between an experimental group and a related control group

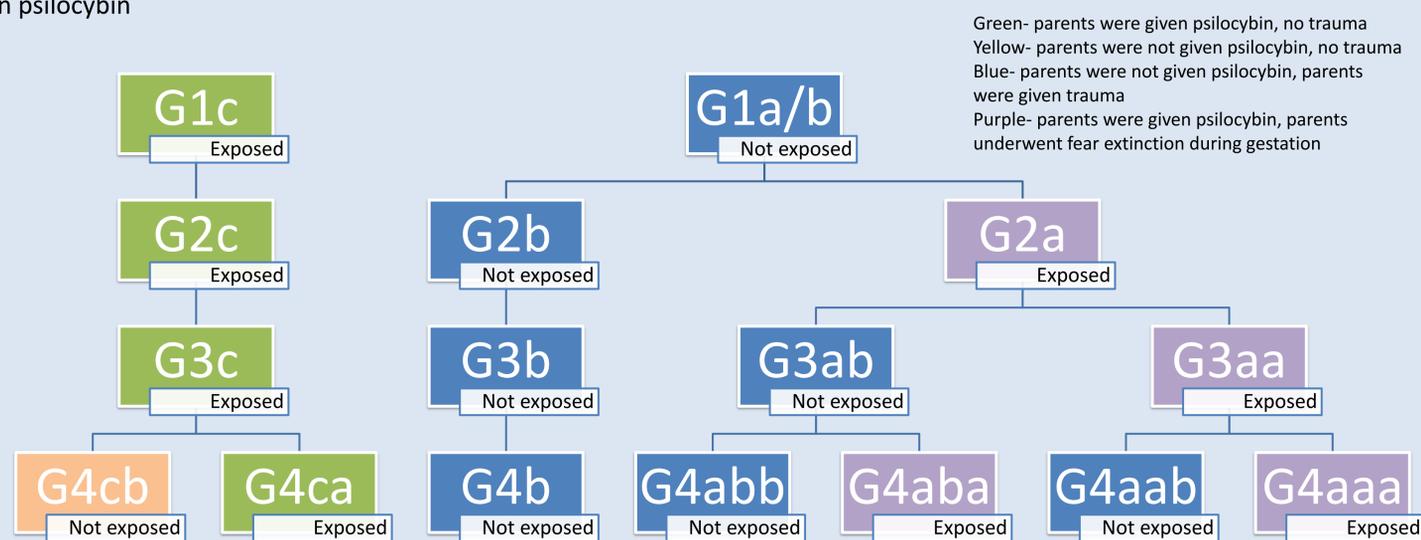


Figure 1: a proposed generational chart of how the mice would be bred. Individuals in the “c” lineage will be exposed to psilocybin before breeding until the 3rd generation. “a” refers to litters born after their parents were exposed to psilocybin and fear extinction. “b” refers to litters born before psilocybin and fear extinction in their parents. Exposure refers to individuals given psilocybin while gestating.

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