AUD AND GLUTAMATE RECEPTORS

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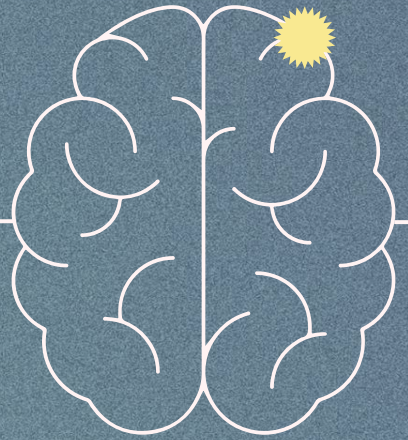
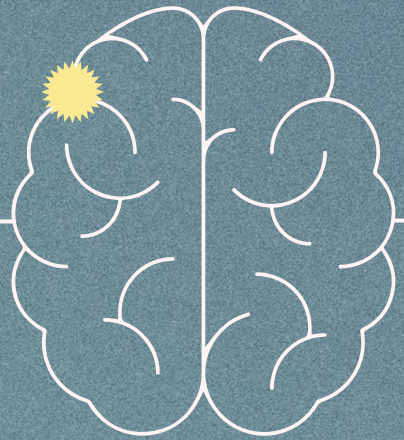




400 000 000

people with alcohol use disorder

700 000

deaths by alcohol related injuries

300 000

deaths by communicable diseases

MAIN QUESTION

How are glutamatergic receptors in the amygdala affected by relapse, withdrawal, and chronic ethanol operant self-administration?

HYPOTHESIS

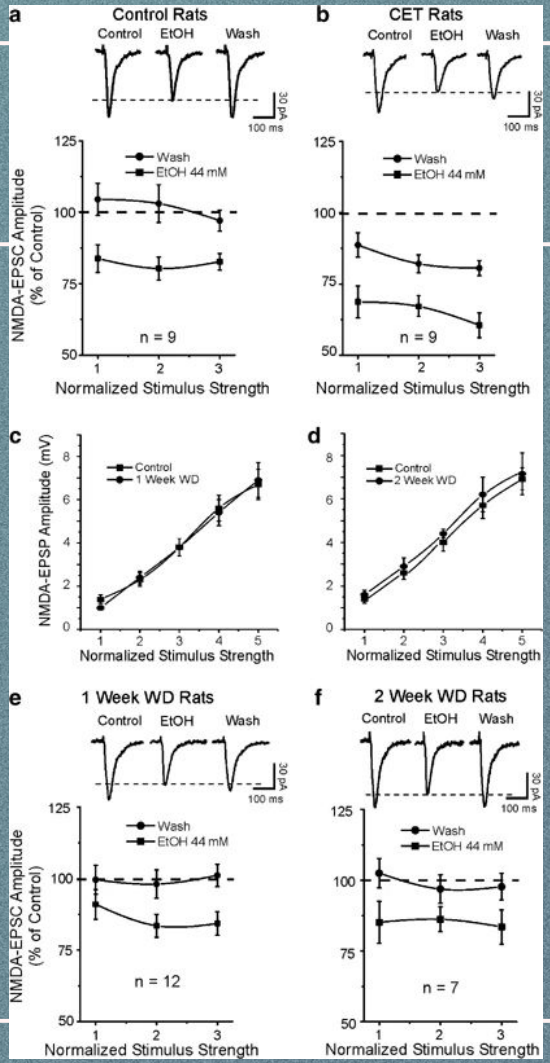
1. If chronic ethanol operant self-administration occurs, then there will be an upregulation of AMPAR and NMDAR in the amygdala because of a lack of excitatory neurotransmission received by the postsynaptic neurons. In the amygdala, this will then lead to an emotional association to ethanol.
2. During withdrawal, there will be a brief upregulation of receptors as the brain continues to register the lack of ethanol. Soon after, there will be an excess of receptors and an increased reception of glutamate which could explain hypersensitivity and negative moods associated with withdrawal.
3. Eventually, downregulation of these receptors will occur as the brain adjusts to maintain synaptic homeostasis
4. If relapse occurs, then AMPAR and NMDAR remain deprived of glutamate and may induce a surge of upregulation. This may result in feelings of guilt, anxiety, and general emotional distress in relation to memory of alcohol.

METHOD

1. Background Research
   - Alcohol Use Disorder (AUD)
   - Glutamate
   - NMDA and AMPA
   - General response to chronic ethanol use, withdrawal and relapse.
2. Research and Data Analysis
   - Effects of ethanol exposure on NMDA receptor and AMPA receptor
     - Genetic Expression
     - Synaptic changes
   - Targeted the amygdala and the prefrontal cortex
3. Applied Research and Proposed Experiment
   - Addressed the gap found in the research
   - Formed an experiment based on the identified gap under the pretense of complete ethical permission and unlimited resources
   - Discussed ethics

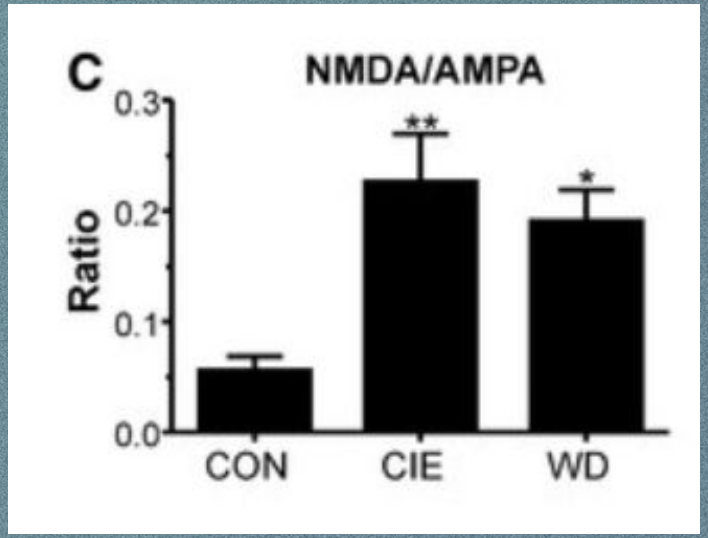
Control system and NMDAR

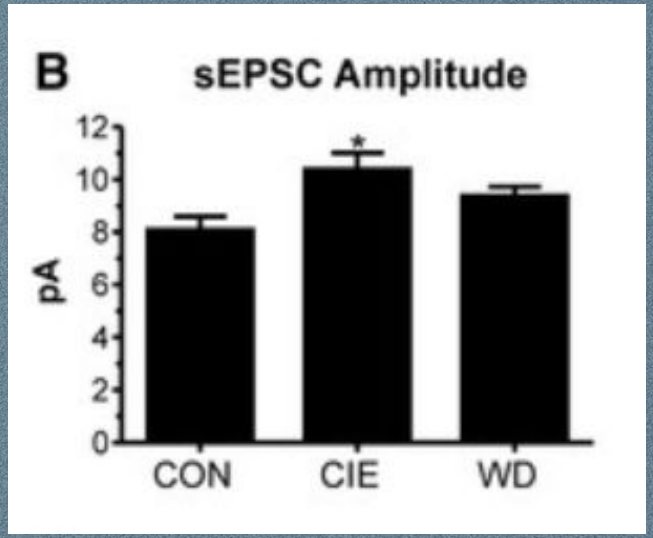
- Created a mathematical model to understand the behavior of NMDAR when exposed to ethanol and ethanol withdrawal
- Regulated negative feedback system with two parts
  - Activity controller: Allow brain's synapses to stay active
  - Density controller: Part that adjusts number of NMDAR



Abstinence and NMDAR in Amygdala

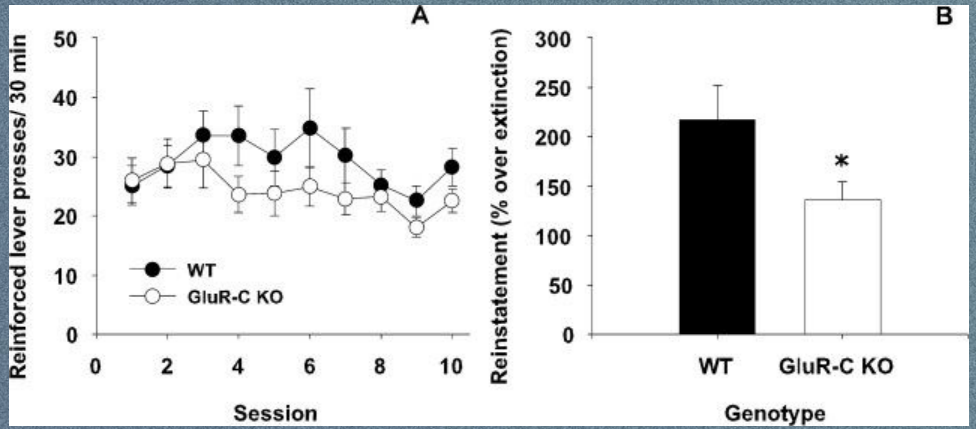
Glutamatergic Synapses in Amygdala

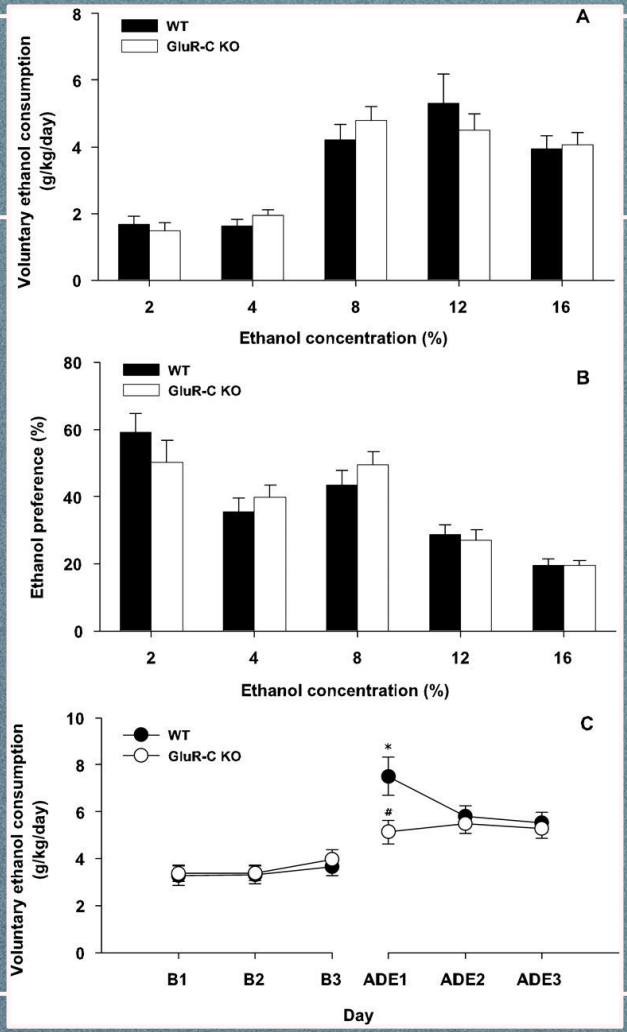




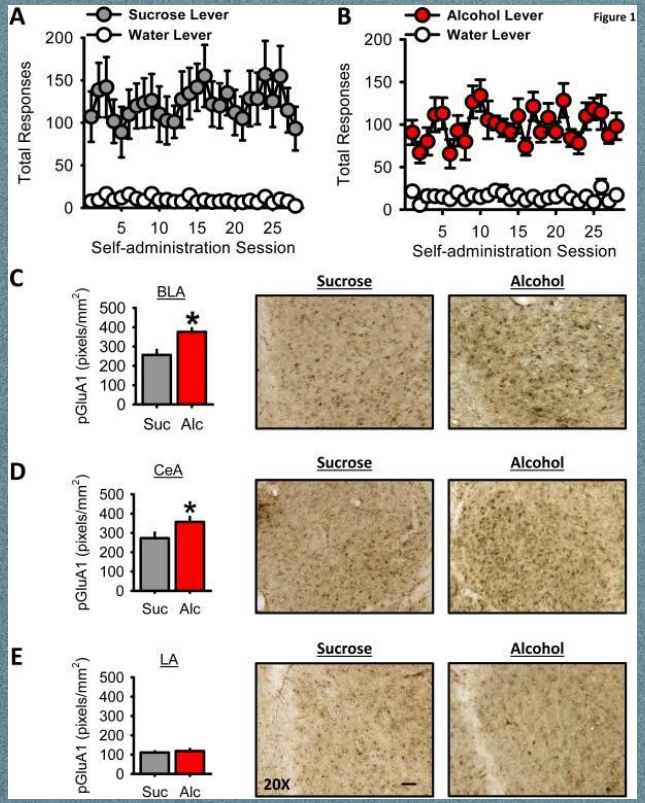
AMPAR AND ADE

AMPAR – α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid-type ionotropic receptors





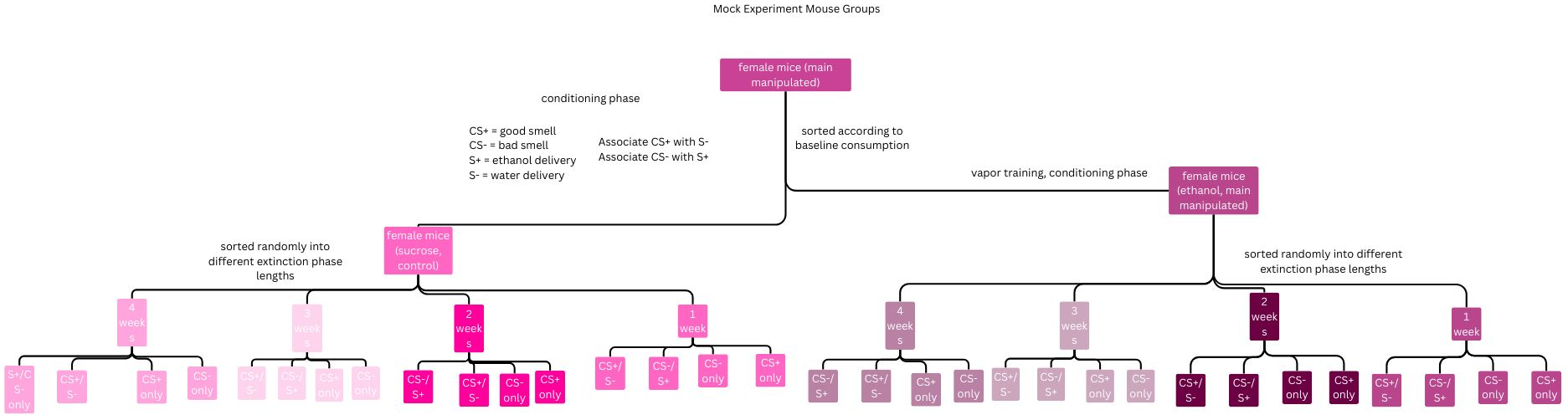
AMPAR AND CaMKII

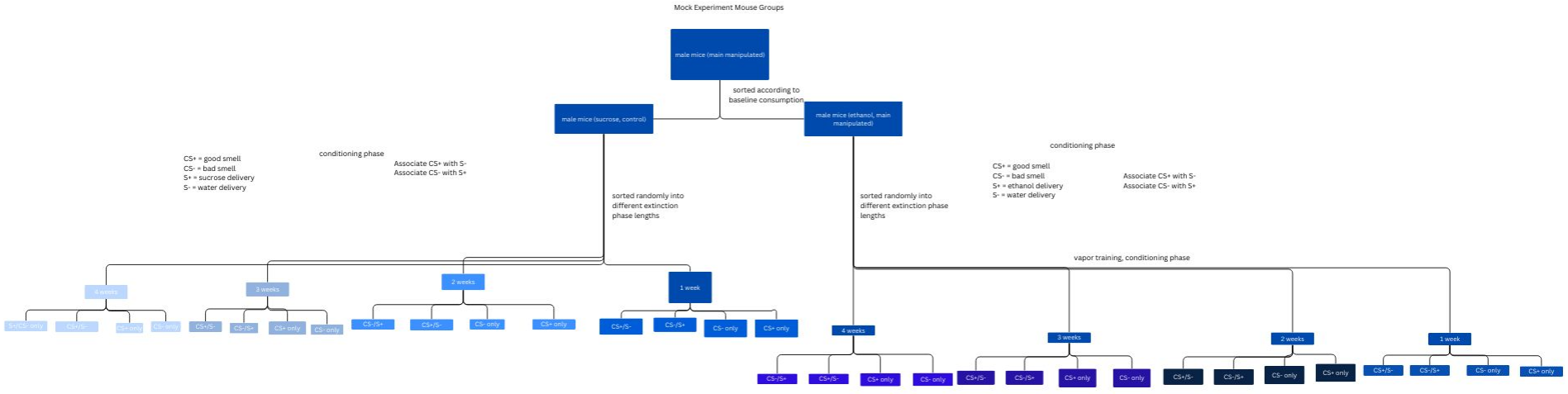


REPRESENTATION IN RESEARCH

2 IN 10

neuroscience experiments use female rodents


Mock Experiment Mouse Groups
female mice (main manipulated)
conditioning phase
CS+ = good smell
CS- = bad smell
S+ = ethanol delivery
S- = water delivery
Associate CS+ with S-
Associate CS- with S+
sorted according to baseline consumption
vapor training, conditioning phase
female mice (ethanol, main manipulated)
female mice (sucrose, control)
sorted randomly into different extinction phase lengths
sorted randomly into different extinction phase lengths
4 weeks
3 weeks
2 weeks
1 week
S+/CS- only
CS+/S-
CS+ only
CS- only
CS+/S-
CS-/S+
CS+ only
CS- only
CS-/S+
CS+/S-
CS- only
CS+ only
CS+/S-
CS-/S+
CS- only
CS+ only
CS-/S+
CS+/S-
CS+ only
CS- only
CS+/S-
CS-/S+
CS- only
CS+ only
CS+/S-
CS-/S+
CS- only
CS+ only
CS+/S-
CS-/S+
CS- only
CS+ only


Mock Experiment Mouse Groups
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sorted according to baseline consumption
male mice (sucrose, control)
male mice (ethanol, main manipulated)
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S+ = sucrose delivery
S- = water delivery
conditioning phase
Associate CS+ with S-
Associate CS- with S+
sorted randomly into different extinction phase lengths
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3 weeks
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CS+/S-
CS-/S+
CS+ only
CS- only
CS+ = good smell
CS- = bad smell
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S- = water delivery
vapor training, conditioning phase

Blood Samples

- Tail-vein sampling method
- Blood will be continually drawn from both control and CET groups and their respective subgroups

Slice Preparation

- Amygdala-isolated brain slices
- Slices examined using electrophysiology and western blotting

CONCLUSION

AMPAR

contributes to overactivity in amygdala when phosphorylation is increased from ethanol

NMDAR

contributes to over activity in amygdala during chronic ethanol use and withdrawal

RELAPSE

Overactivity in the amygdala contributes to relapse

FEMALE LAB RATS

are underrepresented in neuroscience and should be accounted for.

APPLICATION

Eventual research will need to be conducted on humans to be truly effective.

Thank you for listening to our project!