

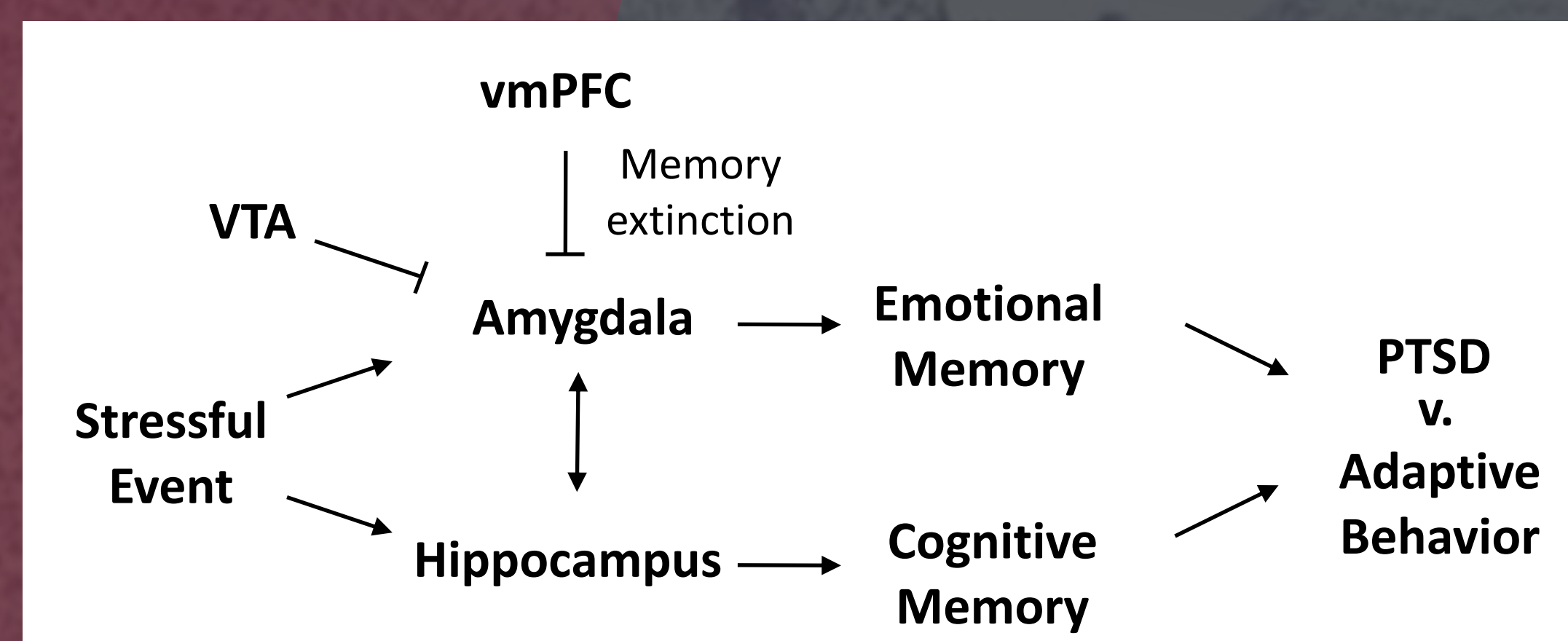
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INTRODUCTION

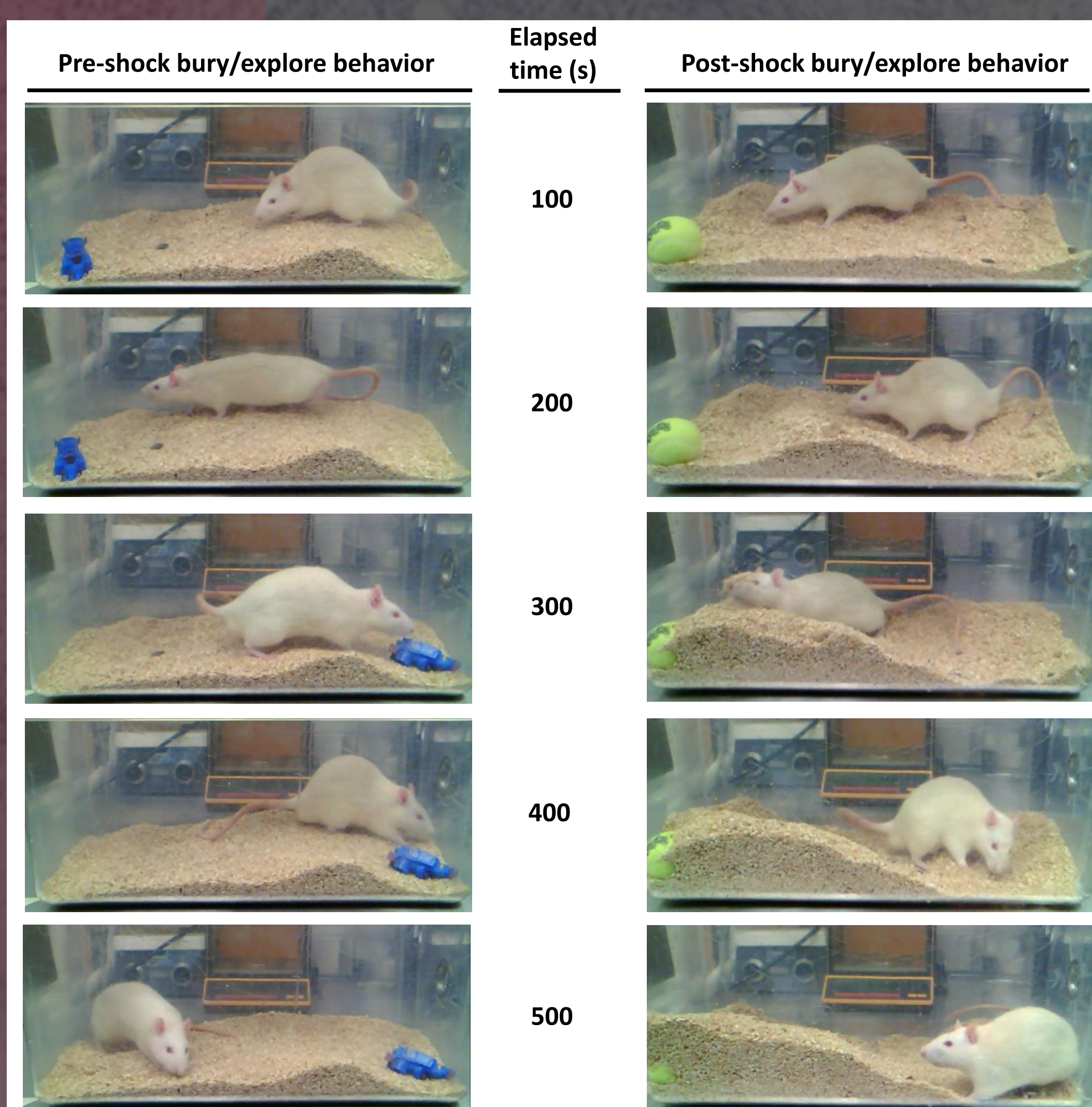
- Posttraumatic stress disorder (PTSD)
- Anxiety disorder occurring after events involving actual or threatened death or injury
- Clinical triad
 - persistent re-experiencing of the event
 - avoidance of stimuli associated with the event
 - increased arousal
- Current treatment includes selective serotonin reuptake inhibitor (SSRI): Paroxetine commonly used
- Proposed neural mechanism of PTSD:



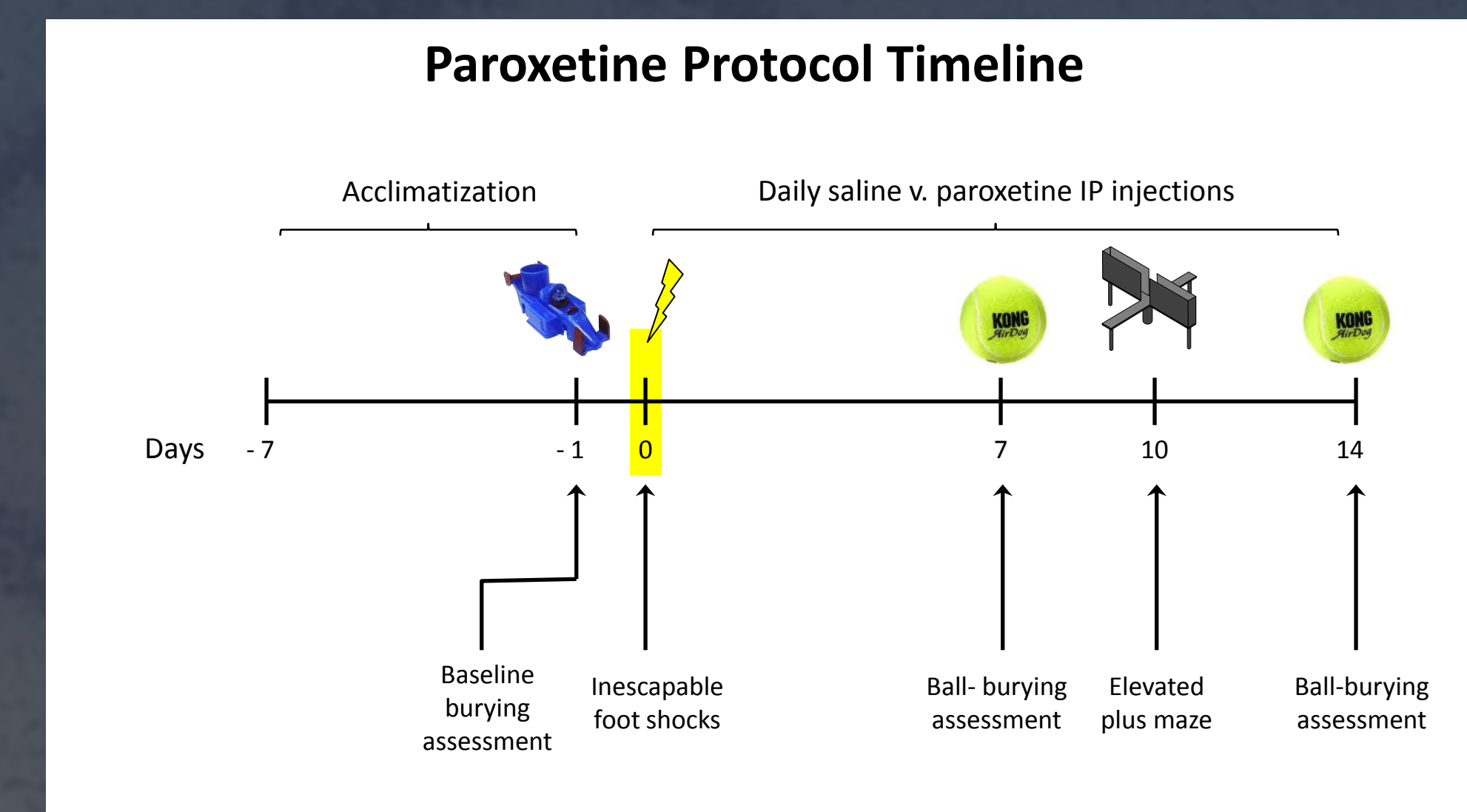
- Deep brain stimulation (DBS)³
- Reversibly inhibits brain targets with high frequency electrical stimulation through an implanted electrode
- DBS to amygdala potential novel treatment of PTSD
- Aim of this study:
 - Compare amygdala DBS to paroxetine in a rat model of PTSD

PTSD RAT MODEL

- Normal rat behavior when presented with a novel object is to explore object:
 - Scratch, sniff, bite, play
- Response to novel object changes after a traumatic event²
 - Initially a rat is presented with a novel object (miniature tennis ball) while subjected to inescapable foot shocks
 - 1 second 2.0 mA shocks every 30 seconds over 5 minutes
 - 1 and 2 weeks later: Rat now buries object
 - Analogous to human avoidance of stimuli associated with traumatic event
 - Burying time is a quantifiable measure of PTSD



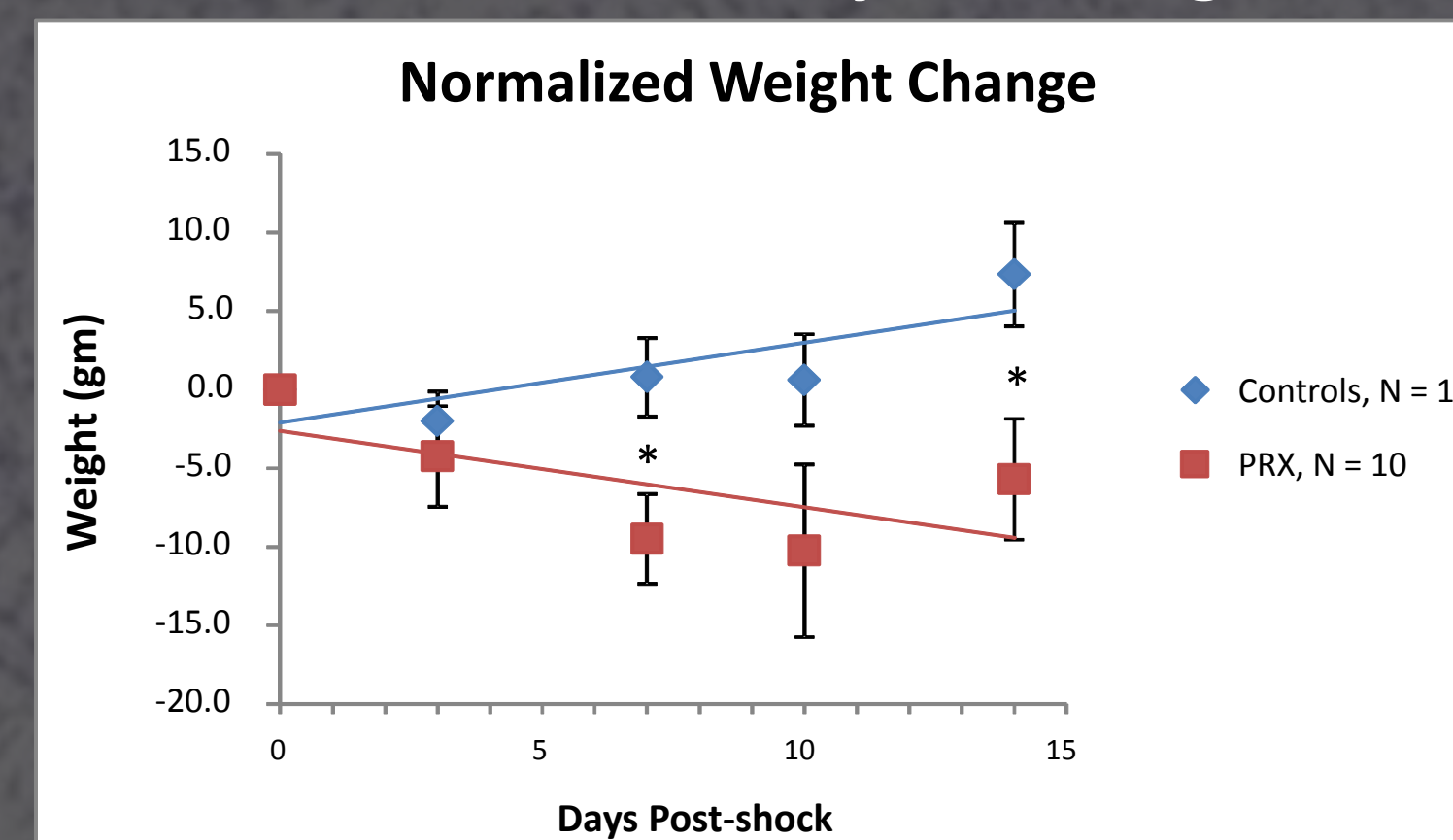
METHODS: PAROXETINE TREATMENT



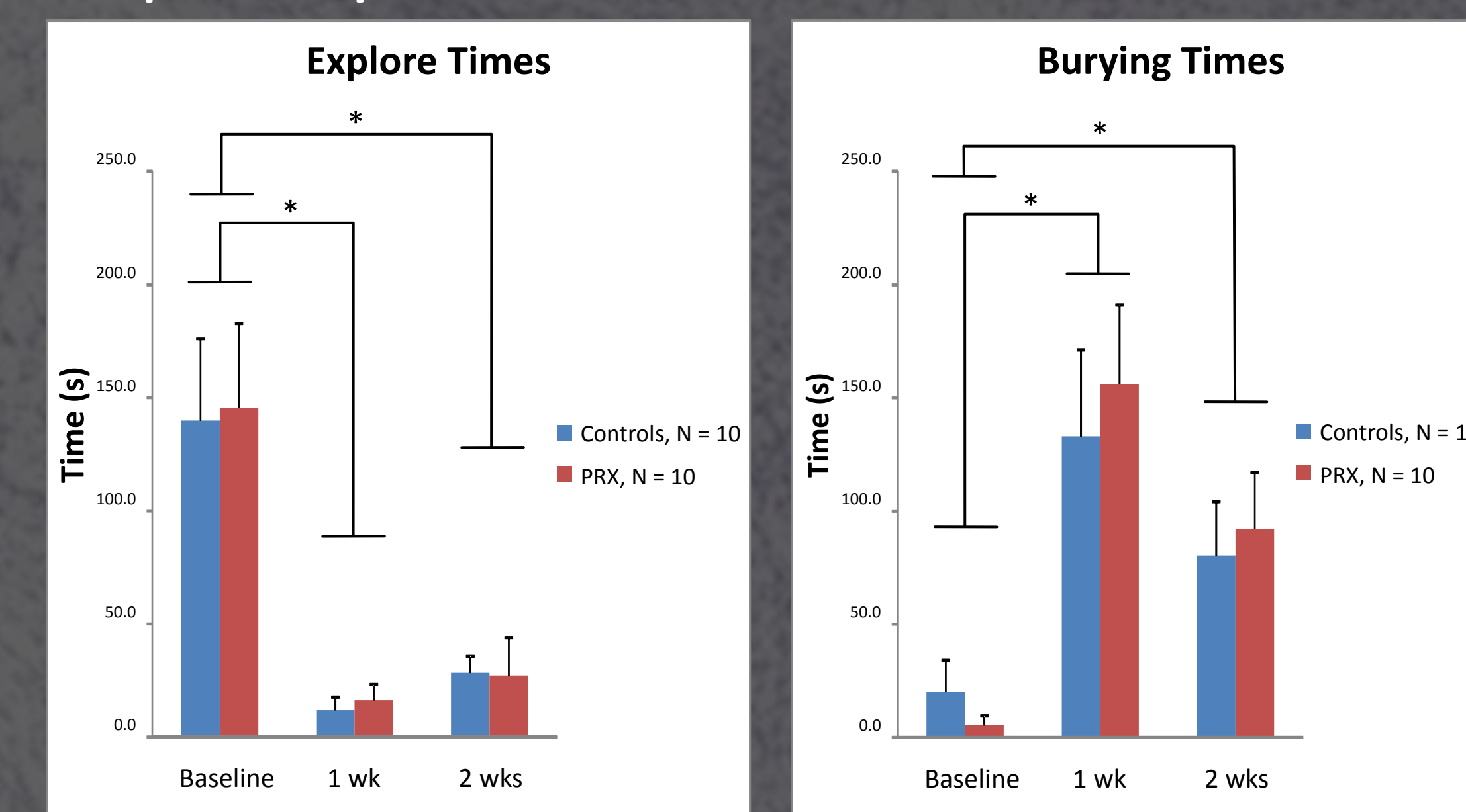
- 20 rats
- Baseline bury/explore assessment with novel object: toy car
- Subjected to inescapable foot shocks in presence of novel object: miniature tennis ball
- Treatment over 2 weeks:
 - Control group: daily intraperitoneal (IP) saline injections
 - Treatment group: daily IP paroxetine 5 mg/kg injections
- Bury/Explore assessment at 1 and 2 weeks post shock with miniature tennis ball
- General anxiety level measure with elevated plus maze at post shock day 10

RESULTS: PAROXETINE TREATMENT

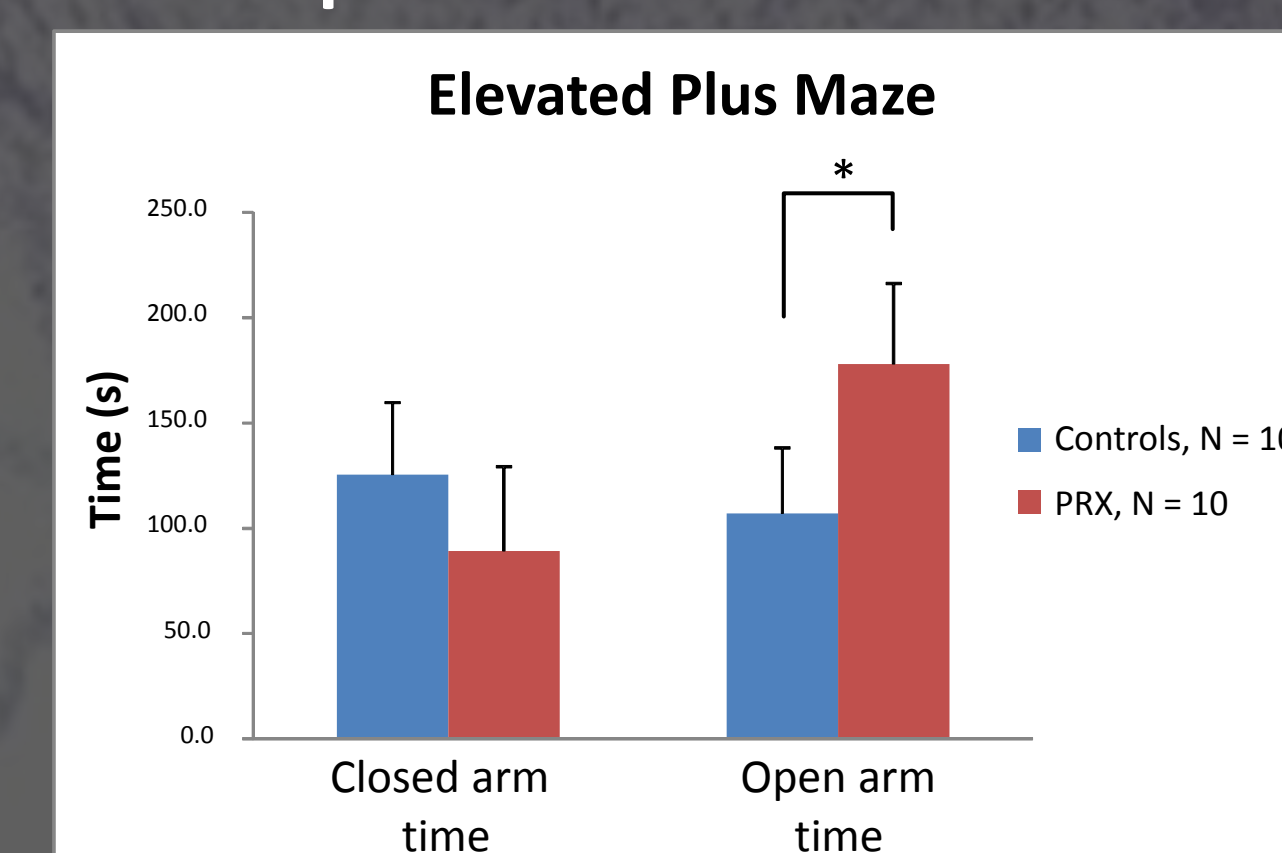
Paroxetine treatment yields weight loss.



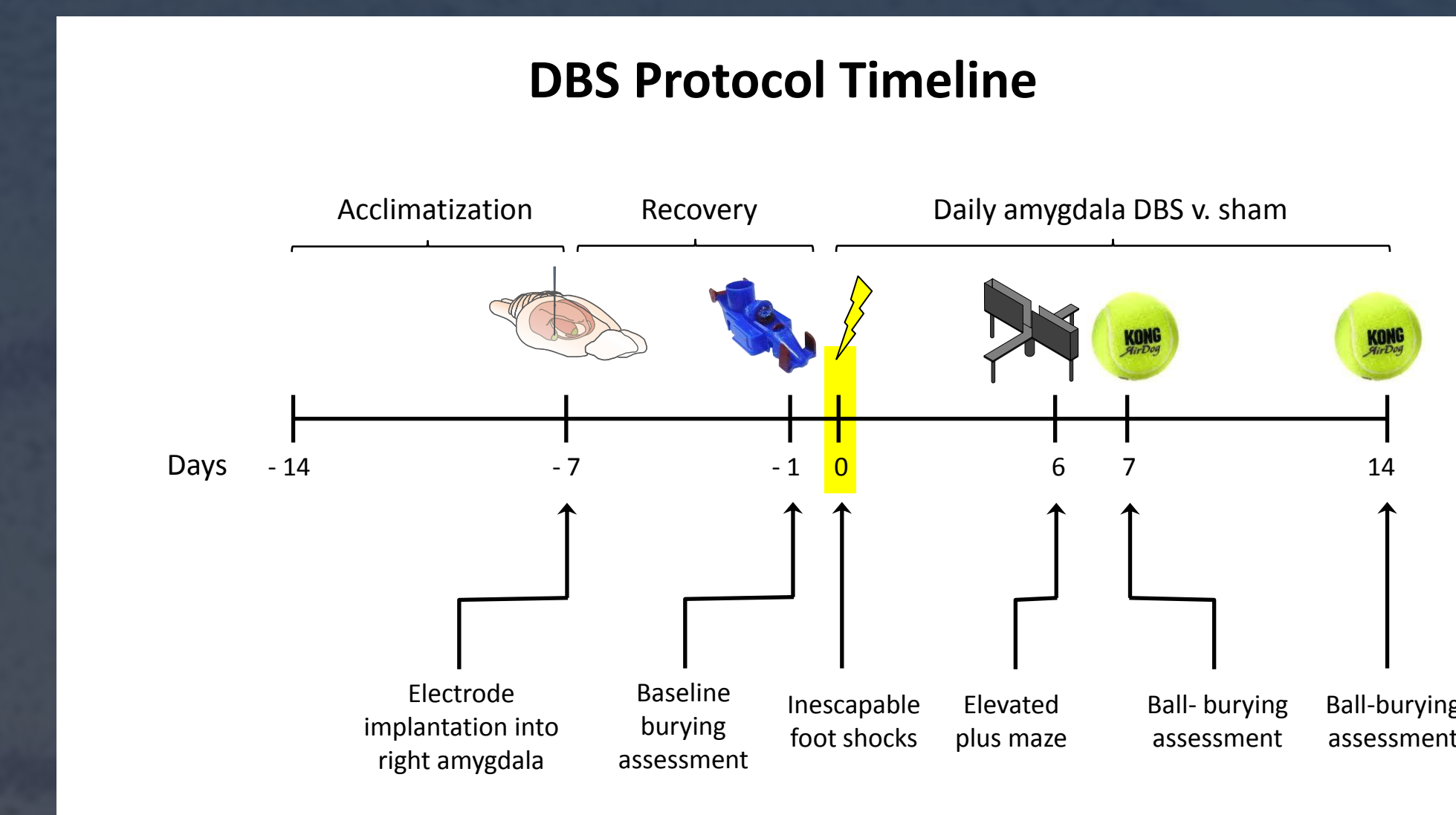
Shocked rats spend less time exploring and more time burying compared to pre-shock. Paroxetine treatment was ineffective.



Paroxetine treated rats spent significantly more time in the open arms than controls.



METHODS: AMYGDALA DBS TREATMENT



- 12 rats implanted with electrodes into right amygdala
- Baseline bury/explore assessment with novel object: toy car
- Subjected to inescapable foot shocks in presence of novel object: miniature tennis ball

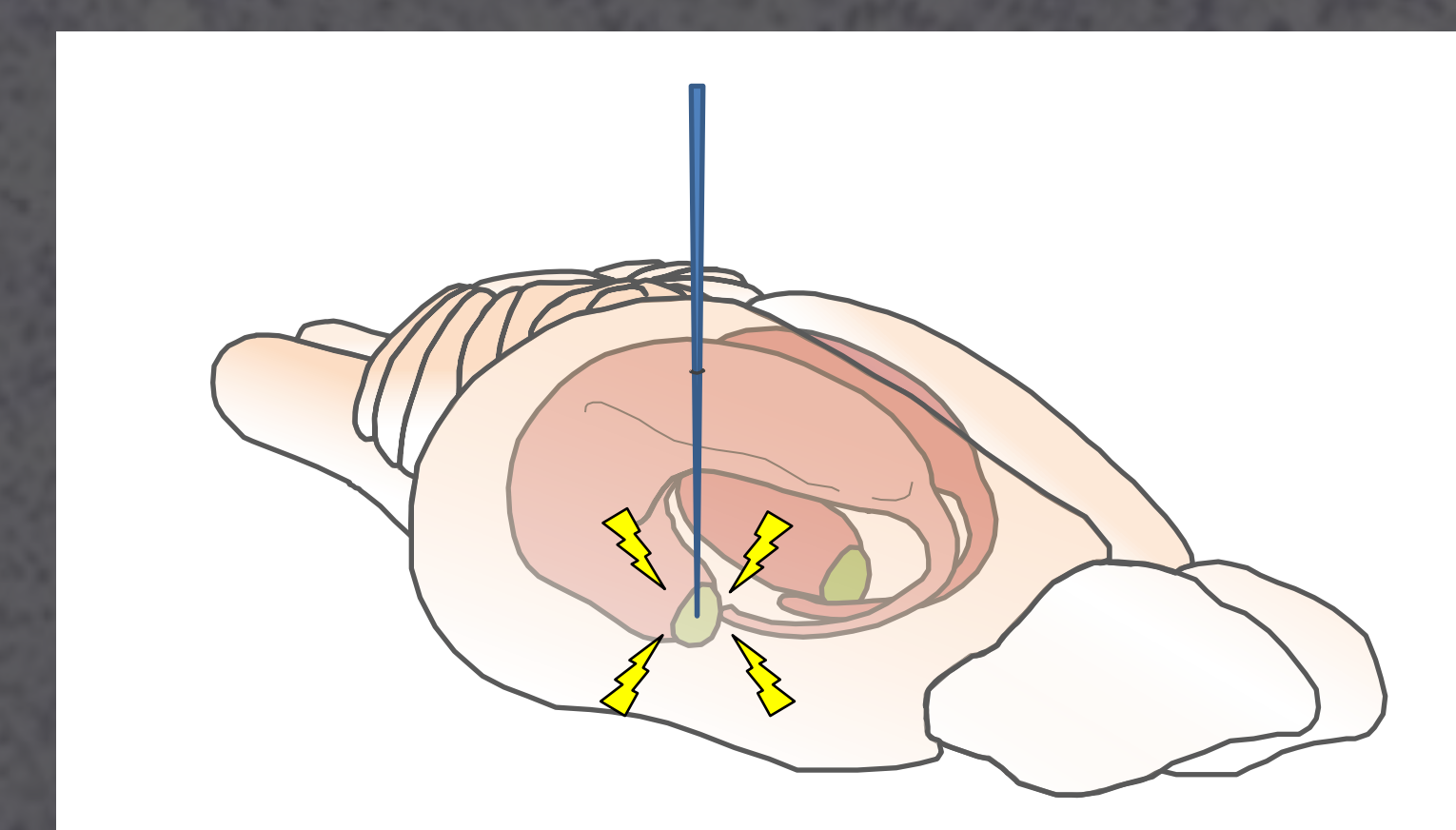
DBS Treatment Schedule (Cross-over Design)

	Post-Shock Week 1	Post-Shock Week 2
DBS-Sham group (N = 6)	Receive DBS therapy	Do not receive DBS therapy
Sham-DBS group (N = 6)	Do not receive DBS therapy	Receive DBS therapy

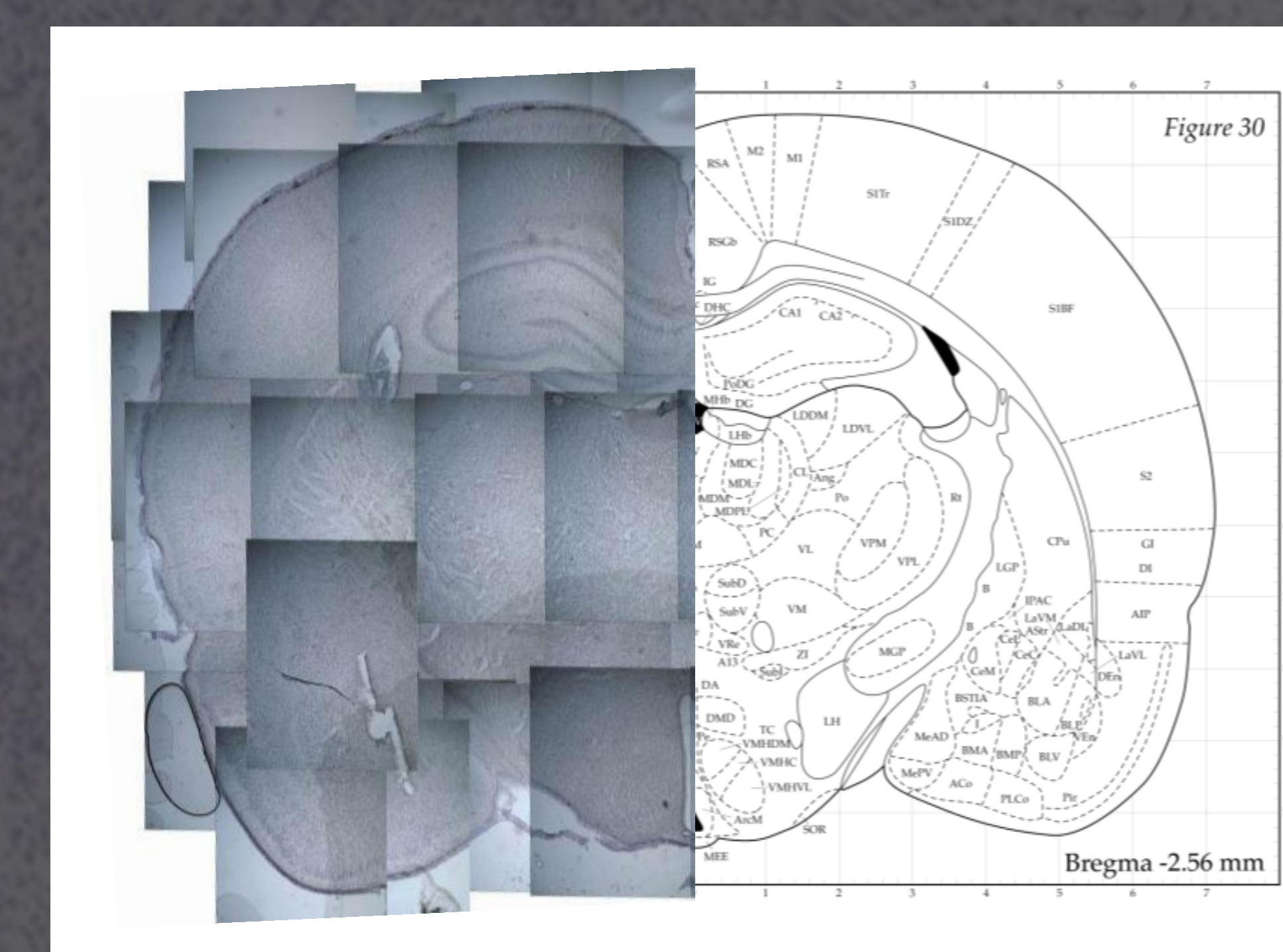
DBS therapy: 2.5 V, 160 Hz, 120 μs pulse width, 4 hours per day

- Bury/Explore assessment at 1 and 2 weeks post shock with miniature tennis ball
- General anxiety level measure with elevated plus maze at post shock day 6

METHODS: DBS ELECTRODE IMPLANT



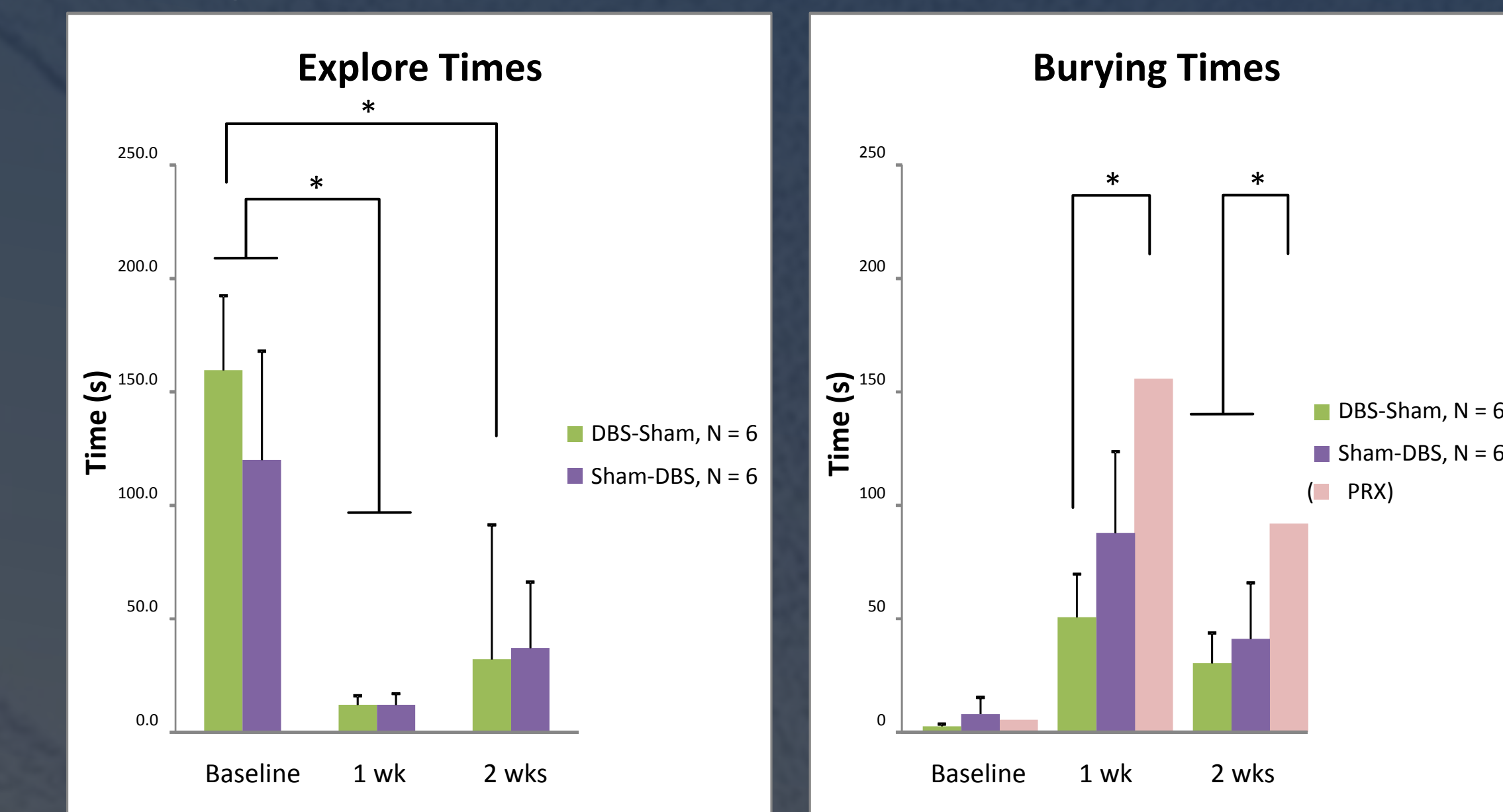
- Target: right basolateral amygdala
- Stereotaxic coordinates:
 - Bregma -2.4 mm, lateral 4.8 mm, 7.2 mm from surface of brain



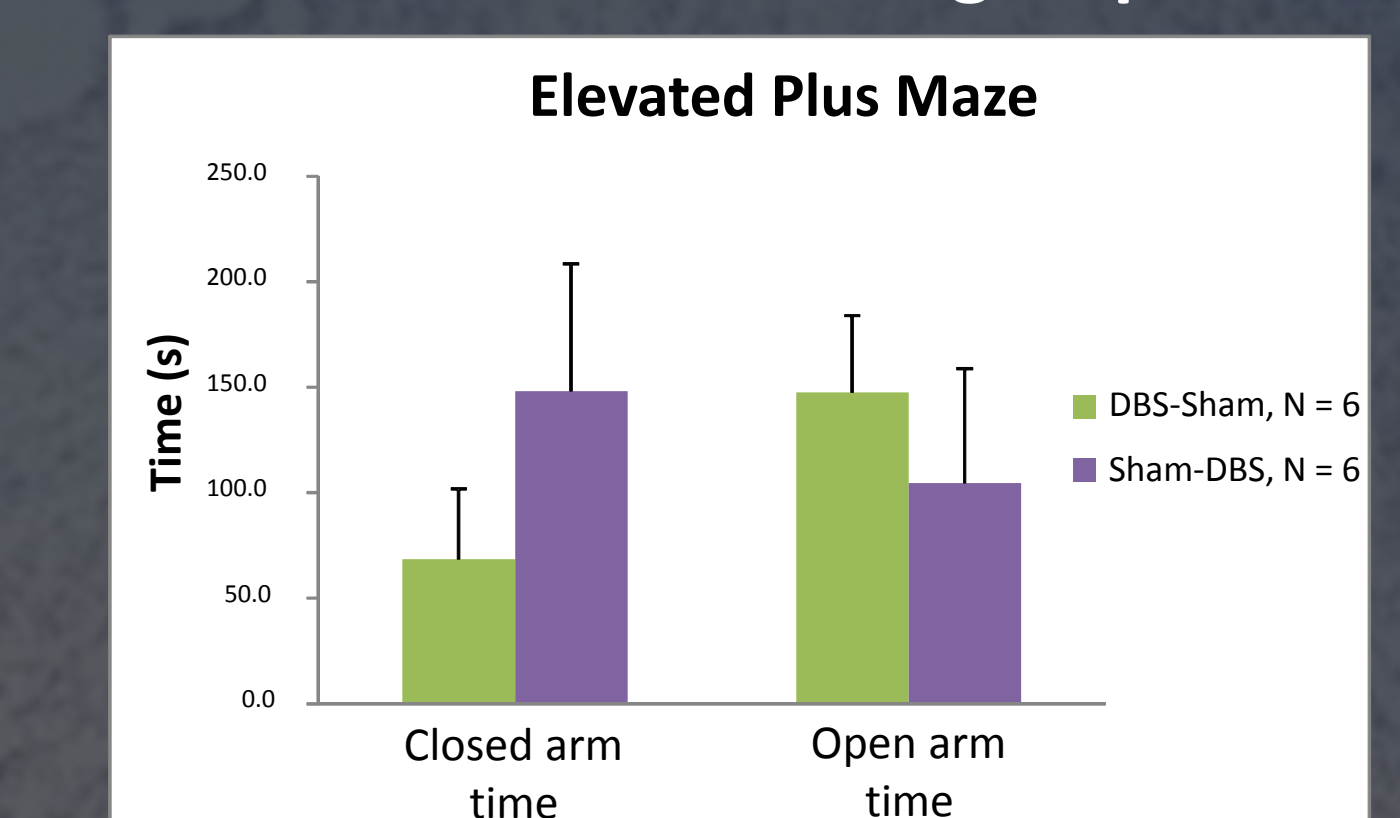
- Electrode location confirmed with histology⁴

RESULTS: AMYGDALA DBS TREATMENT

Shocked rats spend less time exploring and more time burying compared to pre-shock. DBS treatment decreased burying behavior relative to paroxetine treatment.



No significant difference between the two DBS treatment groups.



CONCLUSIONS

- Intraperitoneal paroxetine injections yielded weight loss compatible with previous work
- Paroxetine had no effect on ball burying behavior
 - Paroxetine does not treat the cause of PTSD
- Rats treated with paroxetine spent significantly more time in the open arms of the elevated plus maze
 - Paroxetine lowers generalized anxiety
- Amygdala DBS caused a significant decrease of ball burying behavior
 - Amygdala DBS may be an effective treatment for the cause of PTSD
- There were no significant differences in the elevated plus maze times for the amygdala DBS animals
 - Amygdala DBS does not affect generalized anxiety

ACKNOWLEDGMENTS

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