Effect of Intraperitoneal Paroxetine in a Rat Model of Posttraumatic Stress Disorder

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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:

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 event:
  - 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.

METHODS: AMYGALA 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

RESULTS: AMYGALA DBS TREATMENT

- 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 histology

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

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REFERENCES


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