Introduction

- Current treatments for panic disorder are considered equally efficacious, with approximately 50 to 80% of patients responding to treatment. ¹
- Combination treatment with pharmacotherapy and cognitive behavioral therapy has not been shown to be superior to either alone. ¹
- One new approach that is currently of interest is the augmentation of cognitive behavioral therapy with D-cycloserine, an NMDA receptor partial agonist. ²
- Animal studies have shown that D-cycloserine enhances fear extinction, probably by acting on NMDA receptors in the lateral and basolateral amygdaloid nuclei. ²
- In 2010, Otto and colleagues conducted a pilot study for patients with panic disorder, demonstrating a benefit when administering D-cycloserine alongside exposure-based cognitive behavioral therapy, compared to placebo. ³

Hypothesis

- Compared to cognitive behavioral therapy alone, the administration of D-cycloserine prior to cognitive behavioral therapy will improve clinical outcomes in patients with panic disorder, as evaluated by the Panic Disorder Severity Scale.
- D-cycloserine is expected to be well-tolerated by subjects, demonstrating no significant safety concerns or adverse side effects.
- It is expected that the administration of D-cycloserine prior to exposure-based cognitive behavioral therapy will improve outcomes for patients with panic disorder, as indicated by decreased scores on the Panic Disorder Severity Scale.
- A significant limitation to this study includes a potential lack of generalizability due to the exclusion of a significant proportion of patients with panic disorder.

Specific Aims

- Evaluate the efficacy of D-cycloserine augmentation in patients with panic disorder undergoing exposure-based cognitive behavioral therapy, compared to placebo, as assessed by the Panic Disorder Severity Scale.
- Assess the long-term safety and tolerability of D-cycloserine therapy in patients with panic disorder by examining adverse events.
- The primary outcome measure will be the Panic Disorder Severity Scale score, which will be assessed at baseline, six weeks, one week post-treatment, six weeks post-treatment, and six months post-treatment.
- Based on data from a previous study, a power of 0.8, and an alpha level of 0.05, the desired sample size was calculated to be 250 subjects.
- A paired student’s t test will be used for assessing each arm’s change from baseline. A classic student’s t test will be used for comparing the mean difference between the two arms.

Study Design

- 12-week, multi-center, double-blind, randomized, placebo-controlled clinical trial
- Subjects: patients with panic disorder recruited by clinicians at ambulatory psychiatric centers in the Midwest
- D-cycloserine Group
  - 60-minute exposure-based cognitive behavioral therapy each week
  - 50 mg of D-cycloserine given one hour prior to therapy
- Placebo Group
  - 60-minute exposure-based cognitive behavioral therapy each week
  - 50 mg of placebo mimic given one hour prior to therapy

Methods

Screening

- Structured Clinical Interview for the DSM-IV
- Clinician Global Impression-Severity Scale (CGI-S)

Inclusion Criteria

- Age 18-64
- Meet DSM-IV criteria for panic disorder
- Score at least 4 (moderate) on the CGI-S
- Panic disorder is the most significant current stressor

Exclusion Criteria

- History of:
  - Bipolar disorder
  - Psychosis
  - Delusional disorder
  - Seizures

- Current:
  - Substance abuse or dependence
  - PTSD
  - Major depression
  - Pregnancy or lactation
  - Any serious medical or psychiatric disease

Data Analysis

- The use of D-cycloserine in clinical practice should be encouraged to improve outcomes for patients with panic disorder.

Conclusions and Limitations

- It is expected that the administration of D-cycloserine prior to exposure-based cognitive behavioral therapy will improve outcomes for patients with panic disorder, as indicated by decreased scores on the Panic Disorder Severity Scale.
- D-cycloserine is expected to be well-tolerated by subjects, demonstrating no significant safety concerns or adverse side effects.
- A significant limitation to this study includes a potential lack of generalizability due to the exclusion of a significant proportion of patients with panic disorder.

Future Directions

- Further studies should include a broader population of patients with panic disorder by eliminating exclusion criteria for common co-morbidities.
- Optimal D-cycloserine dosage, duration of therapy, and the timing of administration relative to psychotherapy should be further evaluated.
- The use of D-cycloserine in clinical practice should be encouraged to improve outcomes for patients with panic disorder.