Augmentation of Exposure-Based Cognitive Behavioral Therapy with D-cycloserine in Patients with Panic Disorder

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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, both during a 12-week treatment period and at follow-up assessments.

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.

Data Analysis

➤ 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.

Methods

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

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

Inclusion Criteria
☑ Aged 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

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

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.

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