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D-cycloserine facilitation of cognitive behavioral therapy for delusions in schizophrenia

Jennifer D. Gottlieb, Ph.D.^{1,2}, Corinne Cather, Ph.D.^{2,3}, Meghan Shanahan, B.A.², Timothy Creedon, B.A.², Eric A. Macklin, Ph.D.^{3,4}, and Donald C. Goff, M.D.^{2,3}

¹Dartmouth Medical School Department of Psychiatry/Dartmouth Psychiatric Research Center, 105 Pleasant Street, Concord, NH 03301

²Massachusetts General Hospital Schizophrenia Program, Freedom Trail Clinic, 25 Staniford Street, Boston, MA 02114

³Harvard Medical School, 25 Shattuck Street, Boston, MA 02115

⁴Massachusetts General Hospital Biostatistics Center, 50 Staniford Street, Boston, MA 02114

Abstract

Glutamatergic N-methyl-D-aspartate (NMDA) receptor hypofunction has been proposed as a mechanism underlying psychosis. D-cycloserine, a partial agonist at the glycine site of the NMDA receptor, enhances learning in animal models, although tachyphylaxis develops with repeated dosing. Once-weekly dosing of D-cycloserine produces persistent improvement when combined with cognitive behavioral therapy (CBT) in anxiety disorders. Delusional beliefs can be conceptualized as a learning deficit, characterized by the failure to use contradictory evidence to modify the belief. CBT techniques have been developed with modest success to facilitate such reality-testing (or new learning) in delusional beliefs. The current study evaluated whether D-cycloserine could potentiate beneficial effects of CBT on delusional severity. Twenty-one outpatients with schizophrenia or schizoaffective disorder and moderately severe delusions were randomized in a double-blind cross-over design to receive a single-dose of either D-cycloserine 50mg or placebo in a counterbalanced order on two consecutive weeks 1-hour prior to a CBT intervention involving training in the generation of alternative beliefs. Assessments were completed at baseline, 7 days following the first study drug administration and 7 days following the second study drug administration. Contrary to prediction, there was no significant D-cycloserine treatment effect on delusional distress or severity as measured by the SAPS or PSYRATS. An unexpected finding was an order effect, whereby subjects who received D-cycloserine first had significantly reduced delusional severity, distress, and belief conviction on PSYRATS compared to subjects who received placebo first. However, this finding is consistent with animal models in which D-cycloserine enhances learning only when accompanying the first exposure to training.

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Corresponding Author: Jennifer D. Gottlieb, Ph.D.; Dartmouth Psychiatric Research Center, 105 Pleasant Street, Concord, NH 03301, Jennifer.D.Gottlieb@dartmouth.edu, Phone: 603.271.5747, Fax: 603.271.5265.

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Keywords

NMDA receptor hypofunction; D-cycloserine; Cognitive-Behavioral Therapy; psychosis; delusions; schizophrenia

1. Background and Introduction

Approximately 30% of individuals with schizophrenia continue to experience psychotic symptoms despite treatment with dopamine antagonists. Whereas the formation of delusional beliefs may involve abnormal affective salience resulting from dysregulated release of dopamine¹, the persistence of delusional beliefs can be viewed as a cognitive deficit which results in a failure to correct or “unlearn” the delusional belief in the face of contradictory evidence. Cognitive-behavioral techniques have been developed with modest success to facilitate such reality-testing or “unlearning” of delusional beliefs². In addition, pharmacologic approaches targeting cognitive impairment might also play a role in the treatment of antipsychotic-refractory delusions.

Converging evidence has linked hypofunction of glutamatergic N-methyl D-aspartate (NMDA) receptors to both cognitive deficits and psychotic symptoms in schizophrenia³. It is also well-established that enhancement of NMDA receptor activity by single-dose administration of D-cycloserine improves learning in animal models, including extinction of conditioned fear⁴. At low concentrations, D-cycloserine is a full agonist with twice the potency of glycine at NMDA receptors containing the NR2C subunit, whereas at increasing concentrations partial agonism (approximately 50% activity compared to glycine) at receptors containing NR2A and NR2B becomes prominent⁵. NR2C subunits are involved in fear conditioning, consolidation of fear extinction memory and working memory⁶. NR2C expression was found to be reduced in prefrontal cortex in patients with schizophrenia⁷. In patients with anxiety disorders, D-cycloserine significantly improved outcomes when administered as a single dose prior to once-weekly exposure therapy, a key element of cognitive behavioral treatment for anxiety disorders⁸. In both animal and human studies, D-cycloserine does not improve performance during training; memory effects are only detected when tested 24 hours or more after training, indicating a specific enhancement of memory consolidation, which has been shown to require NMDA receptor activation^{9, 10}.

Consistent with a defect in NMDA receptor function, individuals with schizophrenia exhibit deficits in memory consolidation when tested 24 hours after both procedural memory training¹¹ and conditioned fear extinction training¹² compared to healthy controls. A single dose of D-cycloserine selectively improved memory consolidation in schizophrenia participants as evidenced by enhanced recall of a story from the Wechsler Logical Memory Test after a delay of 7 days, whereas immediate recall was not affected¹³. Repeated daily dosing with D-cycloserine rapidly produces tolerance for memory consolidation in rodents^{14, 15} and did not produce cognitive benefit in schizophrenia patients despite improvement in negative symptoms¹⁶. In contrast, single or intermittent dosing with D-cycloserine may promote neuroplasticity by producing long-lasting changes in synaptic efficiency¹⁷. For example, in a placebo-controlled trial, once-weekly dosing with D-cycloserine for eight weeks produced improvement of negative symptoms measured seven days after the last dose¹³. Of additional potential relevance to the treatment of delusions, D-serine, an agonist at the glycine site of the NMDA receptor, enhanced cognitive flexibility or “reversal learning” in mice performing the Morris Swim Test¹⁸.

We conducted a double-blind placebo-controlled, random-order, single-dose crossover trial of D-cycloserine facilitation of a cognitive behavioral therapy (CBT) exercise designed to

increase participants' capacity to generate alternative explanations for their delusional beliefs. We hypothesized that D-cycloserine, by enhancing learning and cognitive flexibility, would reduce delusional severity and distress, measured one week after the CBT exercise.

2. Methods

The trial is registered as NCT00742079 at ClinicalTrials.gov. The Partners HealthCare IRB approved the protocol.

2.1 Participants

Participants constituted a convenience sample of adult outpatients, ages 18-65 years, at an urban community mental health clinic who met DSM-IV criteria for schizophrenia or schizoaffective disorder (depressed type), and who had experienced persistent delusions despite treatment for at least six weeks with a stable dose of antipsychotic medication. To be eligible, patients had to be medically stable without history of renal insufficiency, dementia, or seizure disorder and without substance abuse or dependence for at least six months. Patients were excluded if they were taking clozapine or had previously engaged in CBT.

All patients met with a research clinician who obtained written informed consent and confirmed the diagnosis based on interview, chart review and consultation with the patient's clinician. Delusional severity was assessed using the Scale for the Assessment of Positive Symptoms (SAPS)¹⁶. Participants were required to score a minimum of 3 ("moderate") on the global measure of delusional severity to qualify at screening. During the screening visit, the three most strongly held delusional beliefs were identified for targeting with the CBT intervention. A medical history and screening laboratory tests were also completed. All participants and study personnel were blind to treatment condition.

2.2 Measures

Baseline measures, including a clinical battery and the Alternative Beliefs Assessment, were repeated prior to study drug administration and the CBT exercise at each of two visits, separated by one week. The SAPS global delusions score was the primary outcome. In addition to SAPS, the clinical battery included the Delusions subscale of the Psychotic Rating Scales (PSYRATS)¹⁷, a six-item scale designed to assess the frequency, intensity, distress, belief conviction, and functional interference associated with delusions, each question scored on a 0 to 4 point scale. Responses to two PSYRATS Delusions items, amount and intensity of associated distress, were summed to reflect a composite "Distress" item. A computerized version of the Probability Reasoning Task - Bead Task,^{18, 19} a decision-making task which requires participants to determine how many beads they would chose from a jar comprised of red and white beads before guessing the color in advance of drawing a new bead, was administered. Individuals with paranoia have been found to gather less data (e.g., select fewer beads) and to express "overconfidence" in their judgments on this task, which is thought to reflect a tendency to "jump to conclusions," a process which may be relevant in the etiology and maintenance of delusional beliefs.^{19,20}

The Alternative Beliefs Assessment (Gottlieb & Cather, unpublished) was performed at baseline to assess cognitive flexibility, or the ability to generate alternative explanations for particular situations. This approximately one-hour assessment used nine vignettes describing social interactions. Three vignettes were neutral in content (e.g., "A man is carrying boxes out of an apartment"), three were negatively-valenced and therefore designed to elicit paranoid interpretations (e.g., "Your phone rings one time late at night") and three were tailored to each participant's specific delusions (e.g., for a patient with a somatic delusion about infection: "You go to your doctor for a check-up and she tells you that your blood test results show no sign of infection."). Participants were asked to generate as many

explanations as they could for each scenario and the number of explanations produced in response to each item was recorded. Three versions of the Alternative Beliefs Assessment per participant were presented in a randomized, counterbalanced order. This assessment was initially completed at baseline without any training or feedback from the assessor. It was also used as the CBT exercise (including training and feedback from the psychologist) at each of two study visits one hour after administration of study drug.

2.3 Procedure

Following the baseline assessment battery, participants received a single oral dose of D-cycloserine 50 mg or placebo double-blind in identical capsules in random, counter-balanced order. One hour later, patients were trained on techniques for producing alternate explanations using several practice vignettes and employing techniques to challenge patients' paranoid appraisals. Participants then completed the Alternative Beliefs Assessment on their own. At Visit 2, one week later, participants again completed the clinical assessment battery. Following the same procedure as their first visit, they then received D-cycloserine or placebo and, one hour later, completed the alternative explanations training and the Alternative Beliefs Assessment. Participants returned for Visit 3 one week after the second CBT session and repeated the clinical battery (see Figure 1).

2.4 Statistical Analysis

Continuous and categorical baseline characteristics were compared by t-test and Fisher's exact test, respectively. Data from each participant's three assessment times (baseline, 7 days following first treatment, and 7 days after cross-over treatment) were analyzed using a linear mixed model with fixed effects for the six combinations of randomized drug order and assessment times and years of education and with random participant-specific intercepts and slopes. Linear contrasts of the cell-mean estimates were used to test for four specific effects: (1) learning effects over each observation interval (change scores over time averaged across randomization order), (2) a first-visit treatment effect (treatment-dependent differences in the change from baseline to the first follow-up assessment, which are thus unconfounded by any carry-over or treatment $\times$ time interaction), (3) an average treatment effect (treatment-dependent differences in change scores averaged over the two 7-day observation intervals, which assumes no carry-over or treatment $\times$ time interaction), and (4) a delayed treatment effect (differences in change from baseline to the final assessment associated with the first treatment received), which is equivalent to an order effect on the final scores. The primary outcome measure was the SAPS global delusions score. The secondary outcome measure was the total score on the Delusions subscale of the PSYRATS. Exploratory analyses additionally were planned using the Conviction and Distress items of the PSYRATS Delusion subscale if the secondary outcome achieved significance. Effect sizes (ES) are the ratio of the a given linear contrast estimate divided by the square-root of the sum of residual and participant-specific variance from a linear mixed model for each outcome measure with fixed effects for each order $\times$ visit combination and participant-specific random intercepts. Note that ES and p-values for a given outcome are not one-to-one since only within-participant variance contributes to uncertainty in drug effects given the cross-over design. Sample sizes required for a future trial of equivalent design were estimated by scaling up the current sample size by the square of the ratio of $(z_{\alpha/2} + z_{\beta})$ over the observed Wald statistics for selected estimates, where z_p is the p-th quantile of the standard normal distribution. Reported p-values are from two-tailed tests without correction for multiple comparisons.

3. Results

Participants were enrolled from Sep 2006 through May 2010. Of 31 enrolled patients, 21 were randomized and 20 received study drug (Figure 2). All 20 participants completed both

sessions of CBT and all assessments. The mean age of participants was 50.2 ± 10.7 years with a range of 28-66 years. Most were Caucasian (65%), male (65%) and unemployed (95%). Seventeen were diagnosed with schizophrenia and three with schizoaffective disorder, depressed type (Table 1). No adverse effects were reported following ingestion of study drug. At baseline, there was no significant demographic or clinical difference between the groups that received D-cycloserine first versus placebo first.

The number of alternative explanations generated on the Alternative Beliefs Assessment significantly increased after the first ($p < 0.001$; ES 1.2) and second ($p = 0.03$; ES 0.49) CBT exercises with no difference between D-cycloserine and placebo conditions ($p > 0.4$) (Figure 3). D-cycloserine did not affect reasoning skills compared to placebo as measured by the Probability Reasoning Task--Bead Task ($p > 0.6$). Change in SAPS global delusions score did not differ between treatment groups (first-visit ES = 0.38, $p = 0.31$; average ES = 0.04, $p = 0.88$). Similarly, PSYRATS total delusions score did not differ between treatment groups (first-visit ES = 0.49, $p = 0.16$; average ES = 0.10, $p = 0.73$). However, a significant order effect was found, such that subjects who received D-cycloserine first had significantly reduced ratings of delusional severity at the end of study compared to subjects who received placebo first (ES 0.77; $p = 0.03$; Figure 4). PSYRATS ratings of delusional distress also exhibited a significant order effect with improvement at end of study in subjects who received D-cycloserine first (ES 0.74; $p = 0.04$, Figure 5) together with improvement on PSYRATS ratings of delusional conviction (ES 1.03; $p = 0.05$).

4. Discussion

Our primary hypothesis, that D-cycloserine would decrease delusional severity and distress when combined with a single session of a CBT exercise designed to increase cognitive flexibility, was not supported by our *a priori* analytic approach, nor did D-cycloserine enhance cognitive flexibility, as measured by the Alternative Beliefs Assessment or reasoning performance on the Bead Task. Performance on the Alternative Beliefs Assessment improved with the CBT exercise regardless of whether subjects were pretreated with D-cycloserine or placebo and did not correlate with change in delusional severity. The striking finding of this study was the significant order effect; subjects who received D-cycloserine prior to the first CBT exercise session experienced significantly greater reductions in delusional severity, distress, and belief conviction at the end of the study than did subjects who received placebo first.

Several factors may have contributed to our pattern of findings. First, the cross-over design, with a one-week washout between intervals, may have been inadequate and led to carry-over effects which would diminish our estimate of treatment effects. Furthermore, the sample size may have been too small to reliably detect D-cycloserine effects compared to placebo on delusional severity, despite effect sizes of 0.4 and 0.5 for SAPS and PSYRATS scores, respectively, after the first CBT exercise. A sample size of $n = 74$, nearly four-fold larger, would have been required for 80% power to detect the observed PSYRATS effect size.

While the significant order effects for response of delusional severity, distress, and conviction were not anticipated, animal experiments examining the roles of NMDA receptors and D-cycloserine in learning provide a possible explanation for this finding. It is well established that D-cycloserine enhances learning in animal models⁴ and that repeated training sessions further enhance learning, consistent with the reduction in delusional severity in subjects who received D-cycloserine first, followed by a second “booster” CBT exercise. However, NMDA activation appears to facilitate learning during the first exposure to new learning only. For example, blockade of hippocampal NMDA receptors has been shown to prevent learning during the first training exposure in several tasks, including fear

conditioning²¹ and conditioned avoidance²², but does not affect subsequent learning if the rat had been pre-exposed to the training or training environment. Similarly, Langton and Richardson²³ found that D-cycloserine facilitated extinction of conditioned fear when administered during the first period of training but had no effect when administered during a second “re-training” session.

Our results are consistent with this model—subjects who received D-cycloserine with their first CBT exercise demonstrated moderate improvement (ES = 0.41 for PSYRATS delusions) in delusional severity after the first session and a further reduction following the second session (ES = 0.22). In contrast, in subjects who received placebo first, the first CBT exercise had no effect on delusions (ES = -0.08) and D-cycloserine subsequently did not enhance response to re-exposure to CBT in the second session (ES = -0.07). While speculative, this possible explanation for our findings would suggest that D-cycloserine should be administered within one hour prior to an initial CBT session for the treatment of delusions to exploit the facilitation of “new learning,” whereas subsequent sessions may reinforce learning and further reduce delusional severity, distress, and conviction, even if unaccompanied by D-cycloserine.

If our findings are replicated, the clinical implications could be substantial since antipsychotic-refractory delusions are generally challenging to treat with standard CBT. A recent meta-analysis by Wykes and colleagues² of 34 trials of CBT in schizophrenia found an effect size for positive symptoms of 0.31 when assessors were masked to treatment allocation. Whereas these trials typically consisted of 20 or more sessions, subjects in our study who received D-cycloserine with the first of two CBT sessions achieved a comparable effect size. Treatment trials of longer duration combining D-cycloserine with CBT are needed to examine the full therapeutic potential of this approach. An important follow-up study design would be provision of a single dose of D-cycloserine prior to an initial CBT session, followed by weekly CBT sessions to further enhance the learning primed by the D-cycloserine. Our findings suggest that within this proposed follow-up design, participants may need fewer CBT sessions than the standard CBT for Psychosis model,² given the potentially substantial priming effects of the initial dose of D-cycloserine prior to the start of the CBT.

The mechanism by which D-cycloserine facilitated CBT also remains to be further elucidated. Cognitive flexibility as measured by the number of alternative explanations generated did not improve with D-cycloserine and did not predict response of delusions, suggesting that D-cycloserine effects on general cognitive flexibility are unlikely to explain the effect. The reductions in delusional severity and distress after two CBT sessions may reflect a direct enhancement of learning similar to D-cycloserine’s facilitation of delayed extinction recall in rodent models. We previously found that individuals with schizophrenia who received a single dose of D-cycloserine prior to listening to a story displayed no improvement in immediate recall but did recall significantly more of the “gist” of the story when tested 7 days later¹³. If the mechanism of D-cycloserine enhancement of CBT similarly involves memory consolidation, therapeutic effects would not be expected to be apparent until 24 hours or more after CBT sessions and would be expected to persist.

In conclusion, the cross-over design of this pilot study produced results that are difficult to interpret due to a significant order effect. However, we did find improvements in delusional severity, distress, and belief conviction after two sessions of a CBT exercise in subjects who received D-cycloserine with the first session. While this was not our a priori hypothesis, this result is consistent with animal studies that have found that D-cycloserine enhances learning only when accompanying the first exposure to training. Larger parallel-group trials of longer duration, which also take into account other important variables, such as negative symptoms

and abstraction deficits, are needed to assess whether this approach may benefit patients with medication-resistant delusions.

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References

1. Kapur S. Psychosis as a state of aberrant salience: a framework linking biology, phenomenology, and pharmacology in schizophrenia. *Am J Psychiatry*. Jan; 2003 160(1):13–23. [PubMed: 12505794]
2. Wykes T, Steel C, Everitt B, Tarrier N. Cognitive Behavior Therapy for Schizophrenia: Effect Sizes, Clinical Models, and Methodological Rigor. *Schizophr Bull*. 2007
3. Goff DC, Coyle JT. The emerging role of glutamate in the pathophysiology and treatment of schizophrenia. *Am J Psychiatry*. 2001; 158:1367–1377. [PubMed: 11532718]
4. Davis M, Ressler K, Rothbaum BO, Richardson R. Effects of D-cycloserine on extinction: translation from preclinical to clinical work. *Biol Psychiatry*. Aug 15; 2006 60(4):369–375. [PubMed: 16919524]
5. Dravid SM, Burger PB, Prakash A, et al. Structural determinants of D-cycloserine efficacy at the NR1/NR2C NMDA receptors. *J Neurosci*. Feb 17; 2010 30(7):2741–2754. [PubMed: 20164358]
6. Hillman BG, Gupta SC, Stairs DJ, Buonanno A, Dravid SM. Behavioral analysis of NR2C knockout mouse reveals deficit in acquisition of conditioned fear and working memory. *Neurobiol Learn Mem*. Feb 2, 2011
7. Beneyto M, Meador-Woodruff JH. Lamina-specific abnormalities of NMDA receptor-associated postsynaptic protein transcripts in the prefrontal cortex in schizophrenia and bipolar disorder. *Neuropsychopharmacology*. Aug; 2008 33(9):2175–2186. [PubMed: 18033238]
8. Norberg MM, Krystal JH, Tolin DF. A meta-analysis of D-cycloserine and the facilitation of fear extinction and exposure therapy. *Biol Psychiatry*. Jun 15; 2008 63(12):1118–1126. [PubMed: 18313643]
9. Kandel ER. The molecular biology of memory storage: a dialogue between genes and synapses. *Science*. Nov 2; 2001 294(5544):1030–1038. [PubMed: 11691980]
10. Wittenberg GM, Tsien JZ. An emerging molecular and cellular framework for memory processing by the hippocampus. *Trends Neurosci*. Oct; 2002 25(10):501–505. [PubMed: 12220877]
11. Manoach DS, Cain MS, Vangel MG, Khurana A, Goff DC, Stickgold R. A failure of sleep-dependent procedural learning in chronic, medicated schizophrenia. *Biol Psychiatry*. Dec 15; 2004 56(12):951–956. [PubMed: 15601605]
12. Holt DJ, Lebron-Milad K, Milad MR, et al. Extinction memory is impaired in schizophrenia. *Biol Psychiatry*. Mar 15; 2009 65(6):455–463. [PubMed: 18986648]
13. Goff DC, Cather C, Gottlieb JD, et al. Once-weekly d-cycloserine effects on negative symptoms and cognition in schizophrenia: An exploratory study. *Schizophr Res*. Dec; 2008 106(2-3):320–327. [PubMed: 18799288]
14. Parnas AS, Weber M, Richardson R. Effects of multiple exposures to D-cycloserine on extinction of conditioned fear in rats. *Neurobiol Learn Mem*. May; 2005 83(3):224–231. [PubMed: 15820858]
15. Quartermain D, Mower J, Rafferty MF, Herting RL, Lanthorn TH. Acute but not chronic activation of the NMDA-coupled glycine receptor with d-cycloserine facilitates learning and retention. *Eur J Pharm*. 1994; 257:7–12.
16. Goff D, Tsai G, Levitt J, et al. A placebo-controlled trial of D-cycloserine added to conventional neuroleptics in patients with schizophrenia. *Arch Gen Psych*. 1999; 56:21–27.
17. Yaka R, Biegon A, Grigoriadis N, et al. D-cycloserine improves functional recovery and reinstates long-term potentiation (LTP) in a mouse model of closed head injury. *FASEB J*. Jul; 2007 21(9):2033–2041. [PubMed: 17351125]

18. Duffy S, Labrie V, Roder JC. D-serine augments NMDA-NR2B receptor-dependent hippocampal long-term depression and spatial reversal learning. *Neuropsychopharmacology*. Apr; 2008 33(5): 1004–1018. [PubMed: 17625504]

Figure 1. Study Design

Figure 2. D-cycloserine facilitation of a cognitive behavioral therapy exercise for delusions in schizophrenia

Figure 3. Total Alternative Beliefs Assessment Responses. (Vertical lines indicate ± 1 SE.)

Figure 4. PSYRATS Delusions Subscale. (Vertical lines indicate ± 1 SE.)

Figure 5. PSYRATS Distress about Delusions Subscale. (Vertical lines indicate ± 1 SE.)

Table 1

Baseline Characteristics of Sample

Demographics	Overall (N=20)	Treatment Group		P-value
		Placebo First (N=9)	D-Cycloserine First (N=11)	
Gender				0.37
Female	7(35%)	2(22%)	5(45%)	
Male	13(65%)	7(78%)	6(55%)	
Age	50.2 (10.7)	51.4(13.0)	49.2(9.0)	0.65
Age of Illness Onset	25.6 (6.4)	29.5(7.3)	23.5(5.0)	0.06
Duration of Illness	23.7(9.8)	19.5(10.1)	26.5(9.4)	0.29
Number of Hospitalizations	8.1 (8.0)	5.3(4.0)	10.0(9.7)	0.22
Years of Education	13.7 (2.7)	14.6 (3.3)	13 (2.0)	0.20
Ethnicity				1.00
African American	4(20%)	2(22%)	2(18%)	
Caucasian	13(65%)	6(67%)	7(64%)	
East/Southeast Asia	3(15%)	1(11%)	2(18%)	
Antipsychotic				1.00
First generation	2(10%)	1(11%)	1(9%)	
Second generation	17(85%)	8(89%)	9(82%)	
Unmedicated	1(5%)	0(0%)	1(9%)	
Diagnosis				0.57
Schizophrenia	17(85%)	7(78%)	10(91%)	
Schizoaffective Disorder	3(15%)	2(22%)	1(9%)	