Comparing the Efficacy of Two Forms of Cognitive Remediation: Strategy-Based vs. Drill-and-Practice Restorative Training for Cognitive Deficits in People with Psychosis

By:
Shyle H. Mehta

Faculty Advisor:
Dr. Matthew M. Kurtz

A Thesis submitted to the Faculty of Wesleyan University in partial fulfillment of the requirements for the Degree of Master of Arts in Neuroscience and Behavior

Middletown, Connecticut May, 2017
Acknowledgements

First and foremost, I would like to thank my advisor, principal investigator, and friend Dr. Matthew M. Kurtz for all the guidance and encouragement he provided me over the past four years. His door was always open to me and I made the most of it. I cannot recall the number of times I popped into Dr. Kurtz’s office to interrupt his work with questions. His invariably optimistic, sunny demeanor made working in his lab even more enjoyable. Without his patient assistance and expertise in the field, this thesis would not be possible.

I would also like to thank Emma Hall and Deja Knight, research assistants in the Schizophrenia Cognition Laboratory, as well as the clinical staff at River Valley Services (RVS) for their contributions to my data collection and analysis. I am especially grateful to Dr. Margaret Meskill, the RVS Training Director, who coordinated with all the clients, interns, and case managers to schedule meetings and testing schedules. This project has been and continues to be a team effort.

I owe all my academic achievements to my parents who made it a priority that their children receive the opportunities they never did. I am humble and grateful for the sacrifices they have made for my education. Their endless encouragement, support, and understanding made this possible.

This thesis is dedicated to all the patients I had the privilege to work with,

who taught me more than I could ever teach them.
# Table of Contents

1. Abstract ......................................................................................................................... iv

2. Introduction: Schizophrenia............................................................................................ 1
   2.1. Symptoms .................................................................................................................. 1
       2.1.1. Positive Symptoms ......................................................................................... 1
       2.1.2. Negative Symptoms ....................................................................................... 2
       2.1.3. Neurocognitive Deficits .................................................................................. 3
   2.2. Diagnosis ................................................................................................................. 5
   2.3. Prevalence and Incidence ......................................................................................... 7
   2.4. Neurochemical Dysfunction ................................................................................... 9
       2.4.1. Dopamine Hypothesis ..................................................................................... 9
       2.4.2. Glutamate Hypothesis ................................................................................... 11
       2.4.3. GABA ............................................................................................................... 12
   2.5. Etiology .................................................................................................................... 14
       2.5.1. Genetic Factors ............................................................................................... 14
       2.5.2. Neurodevelopmental and Environmental Factors ............................................ 16
   2.6. Cognitive Remediation Therapy ............................................................................. 18
   2.7. Present Study .......................................................................................................... 21
   2.8. Hypothesis ............................................................................................................... 22

3. Methods ........................................................................................................................... 22
   3.1. Participants ............................................................................................................... 22
   3.2. Clinical Assessment ................................................................................................. 24
   3.3. Neurocognitive Measures ....................................................................................... 24
   3.4. Social Cognitive Measure ....................................................................................... 28
   3.5. Measures of Function ............................................................................................ 28
   3.6. Baseline and Follow-Up Assessment Procedure .................................................... 30
   3.7. Experimental Conditions ....................................................................................... 31
       3.7.1. PSSCogRehab ................................................................................................. 32
       3.7.2. CogSMART .................................................................................................... 41
   3.8. Statistical Measures ............................................................................................... 43

4. Results .............................................................................................................................. 44
   4.1. Demographic and Clinical Characteristics ............................................................ 44
   4.2. Baseline Performance ............................................................................................. 46
   4.3. Comparing Changes Between Baseline and Follow-Up Performance..................... 48

5. Discussion ......................................................................................................................... 54
   5.1. Evaluating the Results ............................................................................................ 54
       5.1.1. Evaluating the PSSCogRehab Intervention ...................................................... 54
       5.1.2. Evaluating the CogSMART Intervention ....................................................... 55
       5.1.3. Evaluating the Wait-List Control Condition ................................................... 56
   5.2. Evaluating the Hypothesis ...................................................................................... 57
5.3. Limitations and Future Directions................................................. 58
5.4. Conclusion..................................................................................... 61

6. References.......................................................................................... 62

7. Appendix............................................................................................ 77
   7.1. Appendix A: Informed Consent..................................................... 77
   7.2. Appendix B: RVS Release of Information Form ....................... 83
   7.3. Appendix C: HIPAA Release Form............................................. 84
   7.4. Appendix D: RVS Clinical Director Request for Approval......... 87
   7.5. Appendix E: DMHAS Commissioner Approval......................... 88
   7.6. Appendix F: DMHAS IRB Chair Approval................................. 89
1. Abstract

Neurocognitive deficits represent one of the major factors contributing to poor functional outcome in patients with schizophrenia. Therefore, cognitive deficit remediation therapy, a novel form of skills-training intervention that aims to improve neurocognitive deficits, is being implemented more frequently at in- and out-patient psychiatric facilities. Though this practice is increasingly widespread, the type of cognitive remediation therapy used varies greatly. While several forms of cognitive remediation therapy have demonstrated some efficacy, questions remain regarding which cognitive remediation therapies are most efficacious at specified parameters.

One of the oldest and most well-established forms of cognitive remediation therapy is a drill-and-practice restorative computerized cognitive training program called Neuropsychonline Cognitive Rehabilitation Therapy System (PSSCogRehab) (Bracy, 1994). There have been 32 studies conducted investigating the efficacy of this specific computer program. More recently, a strategy-based compensatory cognitive remediation training program called the Cognitive Symptom Management and Rehabilitation Therapy (CogSMART) was developed by Elizabeth Twamley, PhD (Twamley, Vella, Burton, Heaton, & Jeste, 2012). Fifteen studies have investigated the efficacy of CogSMART, but no study has compared the efficacy of a strategy-based compensatory approach to cognitive remediation (CogSMART) to a program of restorative cognitive remediation (PSSCogRehab).

Data was collected from nine patients diagnosed with schizophrenia or schizoaffective disorder. Patients were given a baseline battery of neuropsychological tests, a clinical scale, and functional outcome measures and were then randomly
assigned to one of three conditions (drill-and-practice restorative cognitive remediation, strategy-based compensatory cognitive remediation, or wait-list control). Interventions were administered for three weeks, and then participants were reassessed immediately post-training on several of the neurocognitive tests and one measure of function.

The results demonstrated that 1) neither type of cognitive remediation therapy improved outcome measures, as demonstrated by nonsignificant difference between baseline and follow-up assessments, and 2) neither type of cognitive remediation therapy was more efficacious than the other. However, these findings were probably observed because of the small sample size and short duration of training. Therefore, completion of a longer duration of training with larger cohorts of patients is required to better address the research question at hand.
2. Introduction: Schizophrenia

2.1. Symptoms

Schizophrenia is a severe, psychotic mental illness characterized by a variety of symptoms. Like other mental illnesses, schizophrenia affects the way people feel, think, and behave. The fifth edition of the Diagnostic and Statistical Manual (DSM-5) defines schizophrenia as “a heterogeneous clinical syndrome” because it presents in a variety of ways with different symptoms (American Psychiatric Association, 2013). The hallmark symptom of schizophrenia is psychosis, which is a detachment from reality because of thought and emotional impairments. Since there are other psychotic mental disorders, schizophrenia is often characterized by its three classes of symptoms: positive symptoms, negative symptoms, and neurocognitive deficits.

2.1.1. Positive Symptoms

Positive symptoms entail the presence of abnormal thoughts, feelings, sensory perceptions, and behaviors. Several examples of these include hallucinations, abnormal perceptions, delusions, and disorganized thinking (Saha, Chant, Welham, & McGrath, 2005). Hallucinations are defined as false sensory perceptions that are present in the absence of environmental stimuli. Though most often auditory for schizophrenia, hallucinations can also manifest in all sensory modalities, including vision, somatosensation, olfaction, and gustation (Irmak, 2014). Another common positive symptom in schizophrenia is delusions, which are abnormalities in inferential thinking. These often exist as irrational beliefs, including grandiosity and paranoia (Andreasen,
2000). Often, these present with similar themes, such as paranoia that people are spying on them and/or trying to harm them. Patients often view their hallucinations and delusions as real, which often detrimentally impact patients relationships since others view these symptoms as strange and scary (Fletcher & Frith, 2009). Among patients with schizophrenia, delusions are the most common type of thought disorder. Patients also frequently exhibit disorganized thinking patterns. Disorganized speech entails abnormalities in language production, including incoherence, loose associations (forming connections between ideas that are only tenuously related), and derailment from the relevant ideas regarding the subject in question (Andreasen, 2000). In regards to symptoms pertaining to emotional dysregulation, people with schizophrenia can demonstrate inappropriate affect, which is the expression of emotions that are incompatible with the social context (e.g. laughing during a sad situation). These patients may also demonstrate extreme excitement, which is when appropriate emotions are expressed to an excessive level. Another positive symptom is motor excitement, which entails disorganized movements, including fidgeting, stereotypies, and exaggerated gesticulations.

2.1.2. Negative Symptoms

Unlike positive symptoms, negative symptoms are characterized by reductions in characteristics seen in healthy individuals. The two central examples in schizophrenia include blunted affect and avolition. An individual with blunted affect has drastically diminished facial, vocal, and bodily emotional expression. Moreover,
they may present with alogia, which is reduced speech production. Avolition, on the other hand, refers to diminished motivation to perform activities (Messinger et al., 2011). Within this umbrella category are more specific symptoms, including anhedonia, which is a diminished feeling of pleasure from enjoyable activates, and social withdrawal, which often refers to seeking partial or complete isolation by avoiding social encounters and social situations. Avolition is particularly detrimental to learning and adherence to treatment (Barch, Treadway, & Schoen, 2014).

Though pharmacological treatments can usually treat psychosis associated with schizophrenia (Foussias & Remington, 2010), they are usually less effective or ineffective for treating negative symptoms (Foussias et al., 2014). These symptoms are detrimental to patients’ functional, occupational, and social outcomes (Nguyen et al., 2016). In addition, negative symptoms are associated with quality of life and subjective well-being (Meehl, 2001; Strauss et al., 2013; Strauss, Harrow, Grossman, & Rosen, 2010; Strauss & Gold, 2012); therefore, it is important to address these symptoms. Though the relation between negative symptoms and outcome has been increasingly investigated over the last several years, the underlying biological and psychological mechanisms of these impairments are still not well understood (Fervaha, Foussias, Agid, & Remington, 2014).

2.1.3. Neurocognitive Deficits

Neurocognitive deficits are separate from positive and negative symptoms in that they have a limited relationship to symptoms (Dominguez, Viechtbauer, Simons,
van Os, & Krabbendam, 2009). This class of symptoms has robust associations with functional and vocational impairments (Green, Kern, Braff, & Mintz, 2000; Heinrichs & Zakzanis, 1998). Over 85 percent of patients experience these deficits (Isaac & Januel, 2016), which affect a broad range of cognitive functions, including attention, episodic memory (memory of events), verbal memory (memory of words and linguistic abstractions), working memory, and executive function (Ross et al., 2006).

One example of a neurocognitive deficit is reduced processing speed, which is the inability to adequately fulfill a timed visuo-motor task in an efficient manner. Impairments in working memory and executive functioning are also common among patients with schizophrenia. Working memory is the ability to temporarily store information and manipulate it for successful task completion. Among the various types of memory, working memory includes encoding, maintenance, and manipulation. On the other hand, executive functioning refers to the cognitive function involved in planning, time management, organization, and problem troubleshooting (Ross et al., 2006). Simply put, this set of mental skills are used to complete tasks.

Neurocognitive deficits are observed in at-risk individuals even before their first psychotic episode during what has been labeled the prodromal phase (early stage of schizophrenia characterized by functional decline and subtle symptoms, such as attenuated psychosis) and they worsen with the onset of psychotic symptoms (Shmukler, Gurovich, Agius, & Zaytseva, 2015; Yung et al., 2005). Some evidence suggests that the duration of time that psychosis goes untreated is inversely correlated with cognitive functioning (Scully, Coakley, Kinsella, & Waddington, 1997).
One study proposed that neurocognitive deficits lead to reduced functional capacity by weakening adaptive skills (Bowie & Harvey, 2005). Thus, they are a reliable predictor of occupational impairments (Freedman, 2003). In fact, patients’ performance on tasks that target the neurocognitive domains of attention, processing speed, and working memory significantly predicted patients’ chances of returning to school or work following a nine month clinical stabilization period (Nuechterlein et al., 2011). Additionally, other functional outcomes, namely occupational engagement, residential independence, and self-care are positively correlated with neurocognitive functioning (Harvey & Strassnig, 2012). In regards to cost, poor functional outcome indirectly increases healthcare costs, which, according to one publication, might be as much as triple the amount of treating psychotic symptoms (Harvey & Strassnig, 2012).

Apart from functional outcome, neurocognitive deficits are detrimental to social functioning in patients with schizophrenia (Nakagami, Hoe, & Brekke, 2010; Nakagami, Xie, Hoe, & Brekke, 2008). As in the case of negative symptoms, antipsychotic medications have minimal or no beneficial effect for treating neurocognitive impairments (Keefe et al., 2007), which is in part why research has recently focused more attention to behavioral treatments, such as cognitive remediation therapy to help address these deficits.

2.2. Diagnosis

There are two classification and diagnostic tools used to diagnose schizophrenia and schizophrenia-related disorders, but for the purpose of this thesis, only the fifth
edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) will be considered. The DSM-5 bases the diagnosis of schizophrenia on six criteria. The first criterion, Criterion A, states that at least two of the following symptoms must be present over the course of one month: 1) delusions, 2) hallucinations, 3) disorganized speech, 4) grossly disorganized or catatonic behavior, and 5) negative symptoms (e.g. alogia, avolition, flattened affect). Criterion B entails a diminished level of functioning, specifically social/occupational functioning, in work, interpersonal relations, or self-care. Criterion C specifies that there must be continuous signs of disturbance for at least six months, which includes at least one month of symptoms that meet Criterion A. Criterion D includes the exclusion of schizoaffective disorder as well as mood and bipolar disorders with psychotic features. Criterion E excludes individuals whose disturbance is caused by a general medical condition, such as hyperthyroidism, or substance abuse, which includes medication and illicit drugs. The last criterion, Criterion F, specifies the instances where schizophrenia may be diagnosed when the individual presents with history of autism or other childhood communicative disorders (American Psychiatric Association, 2013).

Compared to the DSM-IV, the DSM-5 does not include different subtypes (e.g. paranoid, catatonic, disorganized, undifferentiated, et cetera) of schizophrenia. Despite these criteria, it should not be mistaken that schizophrenia is in fact “a heterogeneous clinical syndrome” (American Psychiatric Association, 2013). Some researchers have hypothesized that our construct of this mental illness comprises of multiple diseases, as opposed to just one (Keshavan, Nasrallah, & Tandon, 2011). Nonetheless,
schizophrenia has historically been viewed and, hence, treated as a distinct, singular, categorical disorder (Janicak, Tandon, Marder, & Goldman, 2014). Despite advancements in our understanding of schizophrenia, diagnoses are usually made once the disorder has already fully developed (Silverstein, Moghaddam, & Wykes, 2013).

2.3. Prevalence and Incidence

Schizophrenia affects approximately 0.5 to 1 percent of the United States, which is roughly three million people. Worldwide, schizophrenia affects over 20 million people (Hopper, Harrison, Janca, & Sartorius, 2007). According to the World Health Organization (WHO), schizophrenia is the seventh largest cause of disability in the world (WHO, 2001). The lifetime prevalence of schizophrenia is approximately 0.7 percent (Barry, Gaughan, & Hunter, 2012; McEvoy, 2007) while the lifetime prevalence in industrialized countries, such as the United States, Canada, and Australia is 0.9 percent (Frangou, 2008).

Several studies conducted by the WHO have indicated that the symptomatic presentation and incidence of schizophrenia occurs similarly across different cultures (Jablensky et al., 1992). However, the two-year and five-year follow-up portions of these studies demonstrate that people with schizophrenia had better functional outcome, as operationalized and measured by six quantitative dimensions, in India and Nigeria, less economically developed countries. But see (Jablensky & Sartorius, 2008). In addition, more recent studies have found that more economically developed countries had higher estimates of incidence than less economically developed countries.
Another observed environmental factor is that incidence of schizophrenia in urban areas is higher than that in rural areas. Socioeconomic status has not been shown to have an effect on incidence (Saha et al., 2008).

In regards to sex, schizophrenia is marginally more common in men than in women (incidence ratio of 1.4 to 1) (Abel, Drake, & Goldstein, 2010). In addition, the age of onset of schizophrenia is younger for men (around 23 years of age) than for woman (around 28 years of age). For both sexes, onset before 16 years of age or after 50 years of age is uncommon (Lieberman, Stroup & Perkins, 2012)

Comorbidity is commonly seen in patients with schizophrenia (i.e. many patients also suffer from other mental disorders). It is often difficult to determine if depression is its own separate diagnosis or if it is a symptom of schizophrenia. Due to depressive episodes, patients with schizophrenia frequently experience suicidal ideation. Indeed, approximately five percent of deaths related to schizophrenia are suicide and approximately 3,600 people with schizophrenia commit suicide each year in the United States alone. This is even more significant because this rate is over twenty times higher than that of the general population (Meltzer, 1999). These high suicide rates are in large part why the risk of death in people with schizophrenia is two to three times greater than the general population. Unfortunately this mortality gap has only increased over time (Saha et al., 2008).
2.4. Neurochemical Dysfunction

2.4.1. Dopamine Hypothesis

This theory asserts that the psychosis associated with schizophrenia is the result of hyperdopaminergia caused by a dysfunctional dopaminergic system (Toda & Abi-Dargham, 2007). This theory was formulated in the 1960s after researchers revealed that drugs that deplete dopamine diminished psychotic symptoms. During the 1970s and 1980s, post-mortem dissections of brains demonstrated that people with schizophrenia had higher levels of dopamine in their striatum as well as a higher density of D2 receptors (Mackay et al., 1982; Owen et al., 1978). In fact, antipsychotics that antagonize D2 receptors in brain regions – where there is high dopaminergic receptor density (striatum and limbic system) – have successfully reduced psychosis in patients with schizophrenia (Agid et al., 2007; Seeman, 2002; Toda & Abi-Dargham, 2007). This original dopamine hypothesis was criticized for being reductionist. Researchers suggested that atypical dopamine transmission affected different brain regions differently due to the fact that dopamine receptors are differentially distributed in the brain (Davis, Kahn, Ko, & Davidson, 1991). Therefore, these researchers put forth a revised dopamine hypothesis. This entailed the explanations that negative symptoms are caused by diminished dopamine transmission in the prefrontal cortex and that positive symptoms are caused by increased dopamine transmission in the striatum.

Contemporary literature includes a more nuanced understanding of the role of dopamine in schizophrenia. For example, many studies that have focused on the striatum have found higher presynaptic dopamine availability as well as greater
dopamine release into the synapse in this brain region (Howes & Kapur, 2009). In addition, it has been recently hypothesized that D2 receptors are altered in people with schizophrenia (Howes, McCutcheon, & Stone, 2015). There is also evidence that there is an association between the D2 receptor gene and the development of schizophrenia (Ripke et al., 2014). The dopamine hypothesis is not without limitations. While some studies have found heightened D2 receptor density in people with schizophrenia compared to controls, other studies have not (Farde et al., 1990; Martinot et al., 1990). In fact, it has been posited that antipsychotic medications cause increased D2 receptor density, and that this is not a pathophysiological hallmark of the disorder, but rather a response to chronic dopaminergic receptor blockage with lifelong antipsychotic medication treatment (Silvestri et al., 2000).

The dopamine hypothesis has evolved over the years. There is some evidence that indicates that reduced amounts of dopamine in the prefrontal cortex is associated with the neurocognitive deficits associated with schizophrenia. Moreover, D1 receptor upregulation in the prefrontal cortex is a compensatory mechanism (Abi-Dargham et al., 2002). However, studies investigating prefrontal cortex D1 receptors have been inconsistent in their findings (Howes et al., 2015). Notwithstanding these discrepancies, the notion that the mechanism of function of antipsychotic medications is to serve as dopamine antagonists and block striatal D2 receptors has persisted. But it would be reductionist to assert that this is the only mechanism (Howes et al., 2015).
2.4.2. *Glutamate Hypothesis*

Evidence that glutamate might play a role in the pathophysiology of schizophrenia was suggested by the observation of schizophrenia-like symptoms in healthy people who had taken drugs, such as phencyclidine and ketamine, which impact glutamatergic transmission. These drugs are NMDA receptor (ion channel in neurons activated by glutamate) antagonists and, as such, can cause motor deficits, neurocognitive deficits, and psychosis that are similar to schizophrenia symptoms (Javitt & Zukin, 1991). Post-mortem studies of people with schizophrenia have observed diminished NMDA receptor density in the hippocampus and prefrontal cortex (Harrison, 1999). Therefore, researchers began to focus more on NMDA receptor abnormalities (Harrison, 1999). When healthy participants are administered NMDA receptor auto-antibodies, the result is a syndrome similar to schizophrenia. Once these antibodies are removed, this syndrome recedes (Dalmau et al., 2008). This finding provides evidence for the role of NMDA receptors in schizophrenia. Several clinical trials of NMDA receptor modulating drugs have provided even more support for the role of NMDA receptor hypofunction in the production of schizophrenia (Tsai & Lin, 2010). However, there is inconsistency between the studies (Tsai & Lin, 2010).

There is some evidence of morphological changes in the dendrites of glutamatergic neurons in the cortex of people with schizophrenia. However, despite this, there is no evidence to date that there are measurable decreases in glutamate receptors or vesicular transporters (Hu, Macdonald, Elswick, & Sweet, 2015). In fact, there have been studies that provide evidence against decreased glutamate transmission
in schizophrenia. Several studies have used magnetic resonance spectroscopy to measure glutamate levels in the prefrontal cortex, and found that tissue levels of glutamate are, in fact, higher in this brain region in affected individuals (Poels et al., 2014). Though these findings cannot completely discredit theories regarding the involvement of glutamatergic dysfunction in schizophrenia, they certainly suggest that more research needs to be conducted on the role of glutamate.

2.4.3. GABA

GABA dysfunction has been observed in first-episode and non-medicated people with schizophrenia (Wassef, Baker, & Kochan, 2003). In 2012, one study using proton magnetic resonance spectroscopy found that 16 non-medicated people with schizophrenia had increased concentrations of GABA in their medial prefrontal cortices compared to 22 healthy controls (Kegeles et al., 2012). Another study suggested a relationship between GABA levels and stage of illness based on the observation that younger people with schizophrenia had higher concentrations of GABA when compared to older people with schizophrenia (Rowland et al., 2013).

Apart from general GABA concentrations in certain brain regions, studies have investigated the association between GABA inhibitory interneurons containing parvalbumin (PV), a calcium-binding protein, and schizophrenia. There is evidence that dysfunction of these specific GABA interneurons causes an imbalance in the cortex between excitation and inhibition. One study found that people with schizophrenia had less PV-positive GABA interneurons in their frontal cortices (Beasley & Reynolds,
while another study found that affected individuals had diminished levels of mRNA and glutamic acid decarboxylase 67 (GAD67), an enzyme that synthesizes GABA, in their frontal cortices (Beasley, Zhang, Patten, & Reynolds, 2002).

The dopamine and glutamate hypotheses pertain mainly to positive symptoms of schizophrenia. Dysfunctional GABAergic neurotransmission, on the other hand, has been associated with neurocognitive deficits. PV-positive GABAergic interneurons are important for synchronizing neural activity. This neural activity creates gamma frequency oscillations in neural networks (Gonzalez-Burgos, Cho, & Lewis, 2015), including the dorsolateral prefrontal cortex (DLPFC). Simply put, synchronous neural activity in the DLPFC creates gamma frequency oscillations, which seem to be important for neurocognitive processes (Roopun et al., 2008).

Though dysfunctional glutamatergic transmission is mainly involved in producing positive schizophrenia symptoms, it is worth noting that pyramidal glutamatergic neurons play an important role in synchronizing oscillatory neural activity. Hence, dysfunctional glutamatergic transmission could also be associated with neurocognitive deficits. In fact, one study provides evidence that both neurotransmitters are involved in neurocognitive deficits by asserting that dysfunctional glutamate transmission lies upstream from dysfunctional GABA transmission (Homayoun & Moghaddam, 2007). Nonetheless, the neurochemical mechanism by which neurocognitive deficits are produced is still not well understood. This coupled with the fact that current schizophrenia medications do not treat
neurocognitive deficits strongly suggests that future studies should direct efforts towards elucidating this mechanism.

2.5. Etiology

2.5.1. Genetic Factors

Epidemiological studies have consistently found genetic links for schizophrenia. These genetic correlates provide information about people’s risks for developing the disorder. Initially it was thought that genetics contribute to the likelihood for schizophrenia because it was observed that schizophrenia occurs in members within the same families (Cardno et al., 1999). However, this is not good enough evidence to assert that genes are the cause of schizophrenia. This is because members of the same family often live in the same environment; therefore, this observation does not rule out the possibility of environmental factors acting as at least a moderating variable. Thus, researchers have investigated the concordance rates between identical (monozygotic and identical genetic material) and fraternal (dizygotic, but not identical genetic material) twins.

According to the first studies in the late 1990s, genetics accounted for approximately 80 percent of variance for risk of developing schizophrenia (Cannon, Kaprio, Lönnqvist, Huttunen, & Koskenvuo, 1998; Cardno et al., 1999). One study found that monozygotic twins of people with schizophrenia developed schizophrenia 25 to 50 percent of time (Gottesman, 1991). This percentage is considerably higher than that associated with dizygotic twins of people with schizophrenia developing the
disorder (Cardno & Gottesman, 2000). In 2009, another study found that additive genetic effects accounts for approximately 64 percent of variance (Lichtenstein et al., 2009).

The 22q11 deletion syndrome has gained a lot of attention as a possible genetic model of schizophrenia (Swillen, Vogels, Devriendt, & Fryns, 2000). This is a deletion on chromosome 22 that results in developmental abnormalities, specifically in cognition and biological systems (Swillen et al., 2000). This genetic abnormality is seen in 0.025 percent of the population. However, of this small percentage, about a quarter of them experience symptoms that meet the DSM’s criteria for schizophrenia (Walker et al., 2004). In contrast, other studies indicate that only two to ten percent of people diagnosed with schizophrenia have this deletion (Horowitz, Shifman, Rivlin, Pisanté, & Darvasi, 2005; Walker, Kestler, Bollini, & Hochman, 2004), thereby calling into question this deletion’s relevance to schizophrenia considering that the disorder has a relatively much higher incidence.

More recently, in the last several years, researchers have had the technology to target specific loci that are indicative of risk for developing schizophrenia. Due to genomic wide association studies and whole-exome sequencing, researchers have identified 128 common single nucleotide polymorphisms (SNPs) that are associated with increased risk for developing schizophrenia (Kotlar, Mercer, Zwick, & Mulle, 2015). These results have lent insight into the polygeneity of schizophrenia’s biological etiology, which corresponds to its heterogeneity. Among the loci targeted for representing risk, several have been found in genes that encode for the D2 receptor as
well as serotonin receptors (Ibi & González-Maeso, 2015). Moreover, these loci are also found in genes associated with glutamatergic neurotransmission (Ripke et al., 2014) and scaffold proteins at neurons’ postsynaptic density (Purcell et al., 2014). Nonetheless, the 108 most significant SNPs combined account for only 3.4 percent of variance (Ripke et al., 2014). This is surprising given the much higher estimated genetic effects from the study conducted in 2009 (Lichtenstein et al., 2009). Because this area of research is characterized by rapid growth, it is expected that future studies will further elucidate our understanding of the genetic etiology of schizophrenia.

2.5.2. Neurodevelopmental and Environmental Factors

As schizophrenia is viewed as a developmental disorder, the role of one’s environment, especially during upbringing, has been an area of intensifying research interest. During childhood, physical and neuromotor abnormalities can be indications of early pathogenesis (Walker, Savoie, & Davis, 1994; Xu, Chan, & Compton, 2011). This finding supports the theory that the development of schizophrenia has prenatal and perinatal beginnings. This theory hypothesizes that environmental harm and/or genetic neural defects during this early time in a person’s life gives way for pathogenesis (Weinberger, 1987). Postmortem studies have also supported this theory by demonstrating that people with schizophrenia have abnormalities in neuronal migration from subcortical to cortical regions (Kovalenko et al., 2003), a process that occurs during the second trimester of pregnancy, indicating that pathogenesis could occur as early as at the fetal stage. One factor related to genetic mutations that increases
risk for developing schizophrenia is paternal age. The children of fathers 35 years or older are up to three times more at risk for developing schizophrenia (Malaspina, 2001; Wohl & Gorwood, 2007). In addition, in utero malnutrition/malnourishment increases one’s risk for developing schizophrenia. This was observed in pregnant women in regions with famine (St. Clair & He, 2005; Susser & Lin, 1992). Several studies have gone into more detail, claiming that specific vitamin deficiencies (i.e. vitamin A, vitamin D, vitamin B₉) as well as essential fatty acid deficiency are what cause the increased risk in malnourished in utero fetuses (Brown & Susser, 2008). Additionally, the offspring of mothers exposed to viruses and bacteria during their pregnancies significantly are at greater risk of developing schizophrenia (Ibi & González-Maeso, 2015). In fact, the offspring of women who got infected with influenza during their first trimester were shown to have as much as seven times greater risk for developing schizophrenia (Brown et al., 2004). A mother’s compromised/weakened immune system brought on by stress also increases risk (Ibi & González-Maeso, 2015).

Stress also has an effect during childhood; the risk of developing a psychotic disorder is elevated by childhood stress brought on by harmful/detrimental rearing (Rutten & Mill, 2009). There is also some evidence that the risk of developing a psychotic disorder is increased by drug use, including cannabis use, during adolescence. This same study found evidence that cannabis use was also associated to a younger age of onset of a psychotic disorder (Sugranyes et al., 2009).

There is also a considerable amount of evidence that immigration, even in adulthood, might be a social risk factor for developing schizophrenia. One study in
England found that schizophrenia had the greatest incidence in immigrants of African-Caribbean and Black-African origin (Fearon et al., 2006). This finding suggests the notion that stressful experiences might trigger the onset of schizophrenia. If valid and reliable, this would mean that immigrant groups have a much higher risk of developing the disorder (Stilo & Murray, 2010). Further studies provide evidence in support of the notion that immigrants have an increased risk of developing schizophrenia. These include studies conducted with immigrants from Ethiopia to Israel (Weiser et al., 2008), Greece to Belgium (Charalabaki, Bauwens, Stefos, Madianos, & Mendlewicz, 1995), and Suriname to the Netherlands (Selten, Slaets, & Kahn, 1997).

In one study conducted in the United States, African-Americans demonstrated a higher prevalence of schizophrenia relative to other races even though they did not exhibit any significant biological differences (Bresnahan et al., 2007). Therefore, this finding suggests that, along with genetic and stressful events, social factors, such as prejudice and discrimination, could be contributing factors for developing schizophrenia.

### 2.6. Cognitive Remediation Therapy

Learning-based interventions are the lynchpin for cognitive remediation therapy. Their goal is to enhance cognitive functions by targeting compromised areas of cognition through drill-and-practice and strategy-based techniques (Saperstein & Kurtz, 2013). Like the name suggests, drill-and-practice entails repetitive practice of cognitive exercises that become gradually more difficult as performance improves.
Numerous studies have demonstrated the efficacy of drill-and-practice restorative cognitive remediation for improving cognitive deficits in working memory (Kurtz, Mueser, Thime, Corbera, & Wexler, 2015; Kurtz, Seltzer, Shagan, Thime, & Wexler, 2007). An example of a drill-and-practice exercise would be repeatedly presenting participants with a series of numbers on a screen that they must reproduce in the correct order. Upon successful completion of this, the task’s difficulty level gradually increases. As in the case of most cognitive remediation therapies, the prevailing theory is that improvements in one cognitive domain will generalize to improvements in other ones.

Other cognitive remediation programs, namely compensatory cognitive training like CogSMART, use strategy-coaching, which entails having facilitators and patients discuss how recently learned cognitive skills and habits can be used in everyday life (Wykes et al., 2007). For example, facilitators and clients discuss the importance of maintaining a planner to remember tasks and appointments. The hope is that these compensatory cognitive skills and habits generalize to real-world outcomes (Wykes, Huddy, Cellard, McGurk, & Czobor, 2011). Among people with chronic schizophrenia, CogSMART has demonstrated efficacy (Twamley et al., 2012), targeting four domains of cognition, including attention and vigilance, learning and memory, executive functioning, and prospective memory (Mendella et al., 2015). One study conducted on first episode patients with schizophrenia found that CogSMART training could improve social cognition, processing speed, and global cognition (Mendella et al., 2015).
Though different types of cognitive remediation target different aspects of cognition, the ultimate goal is that improvements in any aspect of cognition will generalize so even untrained cognitive abilities will improve and may even generalize to psychosocial outcomes (Saperstein & Kurtz, 2013). Many review articles and meta-analyses have demonstrated the efficacy of various cognitive remediation therapies for enhancing cognitive abilities and psychosocial functioning (McGurk, Twamley, Sitzer, McHugo, & Mueser, 2007; Wykes, Huddy, Cellard, McGurk, & Czobor, 2011). Studies have demonstrated that psychosocial rehabilitation therapies used in conjunction with cognitive remediation therapy have a greater benefit for enhancing functional outcome than cognitive training alone (Janicak et al., 2014).

In regards to changes in the brain, clinical trials have demonstrated that cognitive remediation therapy has been associated with localized alterations to brain activity (Wykes et al., 2002; Wykes, 1998; Wykes et al., 2011) as well as structure (Eack et al., 2010). In fact, one study found that cognitive remediation therapy enhances neural network functioning (Penades et al., 2013). According to one meta-analysis, consisting of nineteen studies, cognitive remediation in schizophrenia promotes plasticity of neural network organization. This analysis demonstrated that cognitive remediation enhances activation in the prefrontal, occipital, and anterior cingulate cortex, areas that have been linked to cognitive abilities (Isaac & Januel, 2016). Another meta-analysis examined the efficacy of working memory training on patients with schizophrenia. The findings of this study indicate that this form of training has neuroplasticity effects, especially in the fusiform gyrus (important for face
recognition), precuneus, and dorsolateral prefrontal cortex (Chan, Shum, Toulopoulou, & Chen, 2008; Elliott, 2003; Li et al., 2015). Considering the detrimental impact of neurocognitive deficits as well as the therapeutic benefit that cognitive remediation therapy confers, it is imperative that research in this field also directs efforts towards improving cognitive remediation therapies and incorporating them into patients’ treatment programs.

2.7. Present Study

The present study was driven by the need for research that investigates the most effective cognitive remediation therapy for remediating neurocognitive deficits in people with schizophrenia by comparing the most commonly studied forms of cognitive remediation: restorative and compensatory therapies. Studies have investigated the efficacy of drill-and-practice restorative therapy as well as strategy-based compensatory therapy, but none have compared the two against each other. The goal of this project was to determine which of the two therapies in question has greater efficacy. More specifically, the study attempted to see which cognitive remediation therapy intervention would produce a greater improvement in cognitive and psychosocial function. Given the impact of neurocognitive deficits on functioning in people with schizophrenia, investigating how to best remediate these deficits has a direct and, hence, tangible benefit on the improvement of clinical care among people with schizophrenia and even other psychosis-related illnesses.
2.8. Hypothesis

The hypothesis was that there would be significant performance improvements between baseline and follow-up test scores in both experimental cohorts and no significant improvement between baseline and follow-up test scores in the treatment-as-usual wait-list control group. In addition, it was hypothesized that the drill-and-practice restorative group would demonstrate more significant improvements in neurocognitive measures while the strategy-based compensatory group would demonstrate more significant improvements in functional outcomes. For the purposes of this thesis, only the preliminary data from a subset of measures collected at three weeks after the onset of interventions will be reported on.

3. Methods

All procedures for the study received relevant approval from the Institutional Review Board (IRB) of the Departmental of Mental Health and Addictions Services (DMHAS) (see Appendix D, Appendix E, and Appendix F) and Wesleyan University.

3.1. Participants

All nine participants were recruited from day programs at River Valley Services (RVS) in Middletown, Connecticut and had to meet DSM-5 criteria for schizophrenia or schizoaffective disorder, as determined by on-site psychiatrists. Due to the difficulty associated with recruiting patients with schizophrenia both in terms of availability and abiding by HIPAA protocol, a convenience sampling method was employed.
Participants were informed of the study by members of the RVS clinical staff. Those who expressed interest in taking part in the study first completed an RVS Release of Information form (see Appendix B) and then met with a member of the study to complete an informed consent (see Appendix A) and HIPAA release form (see Appendix C). All participants were clinically stable, having had their disorder for many years, and were taking antipsychotic medications among other medications for related disturbances, including anxiety and depression.

In addition to having a formal diagnosis of schizophrenia or schizoaffective disorder, participants had to demonstrate adequate proficiency in English given that many of the tests required reading, listening, and speaking. Apart from lack of proficiency in English, exclusion criteria included ongoing substance abuse, uncorrected sensory impairments, intellectual disability, other neurological disorders, and loss of consciousness, as determined by the patient’s medical records and his/her clinician.

Using both patient interviews and medical records, patients’ diagnosis, duration of illness, age of onset, number of hospitalizations, medications, medical conditions, neurological disorders, history of loss of consciousness, and current individual/group counseling were obtained. Patient interviews were also used to determine demographic variables, including age, ethnicity, education, parental education, employment status, and living status. As this study is ongoing, more patients are actively being recruited for participation.
3.2. Clinical Assessment

Structured Clinical Interview - Positive and Negative Syndrome Scale (SCI-PANSS)

A comprehensive, structured interview, the SCI-PANSS is a measure of symptoms among people with schizophrenia. In other words, it is used to measure the extent of positive, negative, and general symptoms. Different sections of the SCI-PANSS correspond to different aspects of these domains of symptoms. The answers provided during the interview were used to assess seven positive, seven negative, and sixteen general symptom items. Each item was rated on a seven-point scale with severity increasing in ascending numerical order (i.e. 1 = least severe; 7 = most severe) (Kay, Fiszbein, & Opler, 1987).

3.3. Neurocognitive Measures

Wechsler Test of Adult Reading (WTAR)

The WTAR was implemented as a proxy for intelligence quotient to estimate Full Scale Intelligence Quotient (FSIQ) scores (Whitney, Shepard, Mariner, Mossbarger, & Herman, 2010). This helped gauge intellectual functioning at baseline, which was necessary to assess if a participant had the intellectual capacity to carry out the remaining tests and to ensure that there were no significant between-group IQ differences. The WTAR requires participants to read 50 words aloud with atypical grapheme to phoneme translations. The words on the list gradually become more difficult and complex. A score of one was given for each correct pronunciation. These numbers were then totaled to determine the raw score, which was then converted to a
standard score using the WTAR manual, which uses data from a normative sample to account for, and factor in, demographic characteristics. The standard score was used to estimate FSIQ (Holdnack, 2001).

*Wisconsin Card Sorting Test (WCST)*

The 64-card card version of the WCST served to assess executive functioning. During this task, the participant must determine a way to sort cards based on a certain characteristic or pattern. In addition, they must be able to adapt and switch to a new sorting method based on simple positive or negative feedback cues from the administrator. The raw score was converted to a standard score using the WCST manual, which uses data from a normative sample to account for, and factor in, age and education level.

*Hopkins Verbal Learning Test (HVLT)*

The HVLT was used to assess verbal learning and memory (Shapiro, Benedict, Schretlen, & Brandt, 1999). During this test, twelve nouns are read aloud by the administrator at a constant pace of one noun per second. The nouns are not random, but rather fall into three distinct categories, such as vegetables, sports, et cetera. The participant’s task is to recall as many of the nouns as they can. This same process is repeated three times (Brandt, 1991). The HVLT also includes a delayed recall trial; however, for this study, only the three learning trials were administered. To obtain the raw score, the sum of all three trials was calculated. The raw score was then converted
to a standard score using the HVLT manual, which uses data from a normative sample to factor in participants’ age. For the follow-up portions of the study, an alternate form of the HVLT was used. That is, participants were given a new set of words to remember to avoid any potential practice effects (Benedict, Schretlen, Groninger, & Brandt, 1998).

*Controlled Oral Word Association Test (COWAT)*

The Controlled Oral Word Association Test (COWAT) was used to test participants’ verbal fluency (Spreen, O., & Strauss, 1998). The facilitator verbally administers this task, which measures participants’ ability to make associations with specific letters. For example, participants were asked to generate words to a phonemic cue, specifically “F,” “A,” “S” as well as to the categorical cue of “Animals.” Each letter and category trial lasted one minute. The raw scores of each trial were summed up and subsequently converted to a standard score using the COWAT manual, which uses data from a normative sample to account for, and factor in, participants’ age, ethnicity, and education level.

*Wechsler Adult Intelligence Scale (WAIS-IV)*

Selected subtests of the WAIS-IV were administered to participants to assess their attention, processing speed, and working memory (Wechsler, 2008). The latter assesses participants’ capacity to store information and manipulate it using mental operations. The subtests used were the Digit Span, Letter-Number Sequencing, and
Digit Symbol. During the Digit Span subtest, the administrator says a certain sequence of digits aloud and the participant’s task is to repeat them back to the administrator in the same order, reverse order, or ascending numerical order. For the Letter-Number Sequencing subtest, the administrator reads aloud a series of numbers and letters, and the participant’s task is to recall the numbers in ascending numerical order followed by the letters in alphabetical order. Lastly, for the Digit Symbol subtest, participants are given a series of numbers and must draw certain corresponding symbols below each of the numbers. The top of the testing sheet has a key that shows which symbols correspond to which numbers, and participants can refer to this key during the subtest. Each subtest has a different standard score, which was obtained by referring to the WAIS-IV manual, which uses data from a normative sample to account for, and factor in, participants’ age.

Memory for Intentions Test (MIST)

The MIST is an assessment of prospective and retrospective memory, which are the capacity to remember to do something in the future and in the past, respectively. During this test, participants are given instructions to do certain tasks at certain times. The participants’ task is to remember to fulfill these tasks at the specified time points (Raskin, 2009). Following this, participants are asked questions about what they had to remember to do. When scoring the MIST, two separate scores were given: one for prospective memory and the other for retrospective memory. The raw scores were
subsequently converted to standard percentiles using the MIST manual that uses data from a normative sample to account for, and factor in, participants’ age and education.

3.4. Social Cognitive Measure

*The Awareness of Social Inference Test (TASIT)*

The TASIT is a computer-based assessment of social perception wherein participants must watch video vignettes one at a time and, following the presentation of each vignette, answer questions pertaining to them. The test is divided into three sections: emotional evaluation, minimal social inference, and enhanced social inference. Each of the video vignettes depicts a real-life social situation involving characters portrayed by professional actors (McDonald, Flanagan, Rollins, & Kinch, 2003).

3.5. Measures of Function

*Social Functioning Scale (SFS)*

The SFS is a measure of function that is like an interview or questionnaire in that it entails the administrator asking questions to the participant about his/her ability to carry out certain tasks as well as how often the participant engages in certain activities. Hence, these questions assess social functioning and areas of impairment. More specifically, they assess interpersonal communication, social engagement, independence, and competence in employment, daily living activities, and recreational activities (Birchwood, Smith, Cochrane, Wetton, & Copestake, 1990).
**Self-Efficacy Scale (SES)**

The SES is a measure of the participant’s belief that he/she has the ability to carry out certain activities. This neurocognitive assessment is administered in the form of a series of questions, each of which is answered on a 0-100 percent scale in 10 percent increments (i.e. 0 = not confident in ability; 100 = very confident in ability). The questions in the SES are categorized into positive, negative, and social subscales (McDermott, 1995). Scoring the SES entailed calculating the mean percentage. That is, the percentages given for each question were totaled and subsequently divided by the total number of questions answered.

**UCSD Performance-Based Skills Assessment (UPSA)**

Select subtests of the UPSA were administered to participants to assess their capability of carrying out everyday tasks (Mausbach, Harvey, Goldman, Jeste, & Patterson, 2007). During this test, participants are told to role-play certain situations that involve performing financial tasks, such as calculating change and writing a check. They are also asked to role-play scenarios that require communicative skills, including rescheduling a medical appointment and calling 4-1-1 to request for information. Based on their performance, participants received a score between zero and twenty, which was subsequently converted to a percentage.
3.6. Baseline and Follow-Up Assessment Procedure

The baseline assessment is broken up into two sessions to avoid participants’ fatigue affecting their performance. Therefore, the first session constitutes completing several neuropsychological measures while the second session entails completing the remaining ones. Following this second session, participants are given a $30 gift card as compensation for their participation. In total, the baseline assessment takes three to four hours.

There are two follow-up assessments for this study: one immediately after the three-month intervention, and another one three months after the post-intervention follow-up (i.e. six months after baseline assessment). Between the two follow-up assessments, participants are not taking part in any aspect of the study; they simply undergo treatment-as-usual. The follow-up assessments are almost identical to the baseline assessment except that the WTAR is not administered. The reason being that the WTAR is simply used as an estimate of FSIQ at baseline to ensure there are no between-group differences. Thus, this assessment is not needed at follow-up.

For the purposes of this thesis, due to a lengthy IRB approval process, only one follow-up assessment was done, and that was after three weeks of intervention. In addition, since participants were unable to be compensated for this three-week follow-up assessment (as it was not specified in the original DMHAS IRB), this three-week follow-up assessment entailed only three neurocognitive tests and one measure of function: HVLT, COWAT, WAIS-IV (Digit Span subtest only), and SFS. These specific assessments were selected for the three-week follow-up because they do not
take very long and were thought to exhibit the most performance improvement among participants.

Figure 1: Original study design

Figure 2: Modified study design

3.7. Experimental Conditions

Following baseline assessment, participants are randomly assigned to one of three groups (PSSCogRehab, CogSMART, or wait-list control) with equal probability
of being assigned to each group. For the wait-list control, participants assigned to this condition (n=3) must wait a period of three months prior to being randomly assigned to one of the two experimental conditions. To avoid any possible bias when randomly assigning participants to groups, a lab member who has never met or assessed the patients conducts the random assignment using an online random number generator. Group assignments are kept hidden from the study personnel who conduct or score follow-up assessments to maintain the single-blinded nature of the study.

3.7.1. PSSCogRehab

The PSSCogRehab computer program was developed by Odie L. Bracy III, PhD in 1994 (Bracy, 1994). Since PSSCogRehab was created, over 32 studies have used it and multiple studies have demonstrated its efficacy (Kurtz et al., 2015, 2007), which is in part why this computer program has continued to be implemented for the past two decades. PSSCogRehab operates on a computer platform, on a website (http://www.neuropsychonline.com) with secure login and password. The interface of the website is intuitive and, hence, user-friendly. The site consists of many exercises, which are categorized by cognitive domain: attention skills, executive skills, memory skills, visuospatial skills, problem solving skills, and communication skills. This study used most of the exercises from the attention skills, memory skills, and executive skills domains.

Three participants were randomly assigned to the PSSCogRehab experimental condition, which entailed three training sessions (45-60 minutes per session) per week
for three months. The first month of training included exercises from the attention skills category (see Table 2), the second month included exercises from the memory skills category (see Table 4), and the third month included exercises from the executive skills category (see Table 6). For the first two months (attention and memory), sessions were divided by sensory modality; therefore, odd numbered sessions focused on the visual modality whereas even numbered sessions focused on the auditory modality. However, each exercise, regardless of modality, used both auditory and visual cues to indicate whether the participant completed the task correctly or incorrectly. Therefore, participants wore over-the-ear headphones whilst completing the exercises.

As seen in Table 2, there were four unique sessions. Upon completion of the fourth session, participants would repeat the session cycle, starting back again at session one. However, each time an exercise was repeated, the difficulty level increased depending on the participants’ prior performance on that exercise. The session cycle repeated three times for a total of twelve sessions; therefore, each of the four unique sessions was completed three times.
<table>
<thead>
<tr>
<th><strong>PSSCogRehab</strong></th>
<th><strong>Attention</strong></th>
<th><strong>Exercise</strong></th>
<th><strong>Description</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple Visual Reaction (fixed)</td>
<td></td>
<td></td>
<td>Measure of sustained attention and reaction time (RT) where participants click when a square appears. Square changes color depending on reaction time and accuracy.</td>
</tr>
<tr>
<td>Simple Visual Reaction (random)</td>
<td></td>
<td></td>
<td>Measure of sustained attention, RT, and covert attention where participants focus their gaze on the center of the screen and click when a square appears in their periphery. Square changes color depending RT and accuracy.</td>
</tr>
<tr>
<td>Choice Visual Reaction (fixed)</td>
<td></td>
<td></td>
<td>Measure of selective attention and RT where participants click when a square of a specified color appears. Participants are instructed to not click when a square of another color appears. A torus on the screen changes color depending on RT and accuracy.</td>
</tr>
<tr>
<td>Choice Visual Reaction (random)</td>
<td></td>
<td></td>
<td>Measure of selective attention, RT, and covert attention where participants focus their gaze on the center of the screen and click when a square of a specified color appears in their periphery. Participants are instructed to not click when a square of another color appears. A torus on the screen changes color depending on RT and accuracy.</td>
</tr>
<tr>
<td>Simple Auditory Reaction (fixed)</td>
<td></td>
<td></td>
<td>Measure of sustained attention and RT where participants click when they hear a sound (at random intervals). A square on the screen changes colors depending on RT and accuracy.</td>
</tr>
<tr>
<td>Simple Auditory Reaction (random)</td>
<td></td>
<td></td>
<td>Measure of sustained attention and RT where participants click when they hear a sound (at random intervals). Sound is emitted from left speaker, right speaker, or both. A square on the screen changes colors depending on RT and accuracy.</td>
</tr>
<tr>
<td>Choice Auditory Reaction (fixed)</td>
<td></td>
<td></td>
<td>Measure of selective attention and RT where participants click when they hear a sound at a specified frequency. Participants are instructed to not click when they hear a sound of another frequency. A torus on the screen changes colors depending on RT and accuracy.</td>
</tr>
<tr>
<td>Exercise</td>
<td>Description</td>
<td></td>
<td></td>
</tr>
<tr>
<td>----------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Choice Auditory Reaction (random)</td>
<td>Measure of selective attention and RT where participants click when they hear a sound at a specified frequency. Participants are instructed to not click when they hear a sound of another frequency. Sound is emitted from left speaker, right speaker, or both. A torus on the screen changes colors depending on RT and accuracy.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Divided Visual Attention I</td>
<td>Measure of divided attention, sustained attention, RT, and working memory where participants view a series of rapidly changing numbers, click when a square appears on the screen, and subsequently indicate what the last number in the series was. Square changes color depending on RT and accuracy.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visual Reaction Differential Response</td>
<td>Measure of shifting attention, RT, and covert attention where participants focus their gaze on the center of the screen and press the left or right arrow key depending on if the stimulus appears on the left or right side of the screen. Average RT is shown throughout.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visual Discrimination Differential Response</td>
<td>Measure of shifting attention, RT, and covert attention where participants focus their gaze on the center of the screen and press the left or right arrow key depending on if the square, which appears at random locations, is blue or red. The left side of the screen is framed in blue whereas the right is framed in red. A torus on the screen changes colors depending on RT and accuracy.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Divided Auditory Attention I</td>
<td>Measure of divided attention, sustained attention, working memory, and RT where participants listen to a series of rapidly changing numbers, click when a sound is emitted, and subsequently indicate what the last number in the series was. A torus on the screen changes colors depending on RT.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simultaneous Multiple Attention</td>
<td>Measure of sustained attention, divided attention, selective attention, and RT where participants watch a series of moving colored blocks and click on the one that matches the color of the center block when it lines up with the center block.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table 1:** Descriptions of the PSSCogRehab attention skills exercises
<table>
<thead>
<tr>
<th><strong>Session 1</strong></th>
<th><strong>Session 2</strong></th>
<th><strong>Session 3</strong></th>
<th><strong>Session 4</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple Visual Reaction (fixed)</td>
<td>Simple Auditory Reaction (fixed)</td>
<td>Divided Visual Attention I</td>
<td>Divided Auditory Attention I</td>
</tr>
<tr>
<td>Simple Visual Reaction (random)</td>
<td>Simple Auditory Reaction (random)</td>
<td>Visual Reaction Differential Response</td>
<td>Simultaneous Multiple Attention</td>
</tr>
<tr>
<td>Choice Visual Reaction (fixed)</td>
<td>Choice Auditory Reaction (fixed)</td>
<td>Visual Discrimination Differential Response</td>
<td></td>
</tr>
<tr>
<td>Choice Visual Reaction (random)</td>
<td>Choice Auditory Reaction (random)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table 2:** Attention skills curriculum for the first month
<table>
<thead>
<tr>
<th><strong>PSSCogRehab</strong></th>
<th><strong>Description</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Memory Exercise</strong></td>
<td>Measure of short term memory where participants watch numbers being presented one at a time and then recall them.</td>
</tr>
<tr>
<td>Sequenced Recall {Digits [visual]}</td>
<td>Measure of short term memory where participants watch graphics being presented one at a time and then recall them.</td>
</tr>
<tr>
<td>Reversed Recall {Digits [visual]}</td>
<td>Measure of working memory where participants watch numbers being presented one at a time and then recall them in reverse order.</td>
</tr>
<tr>
<td>Sequenced Recall {Graphics [visual]}</td>
<td>Measure of short term memory where participants watch numbers being presented one at a time and then recall them.</td>
</tr>
<tr>
<td>Colormatch</td>
<td>Measure of short term memory where participants match face-down cards based on color. Cards can be turned face-up (two at a time), but only for a short duration.</td>
</tr>
<tr>
<td>Sequenced Recall {Digits [auditory]}</td>
<td>Measure of short term memory where participants hear a series of numbers and then recall them.</td>
</tr>
<tr>
<td>Reversed Recall {Digits [auditory]}</td>
<td>Measure of working memory where participants hear a series of numbers and then recall them in reverse order.</td>
</tr>
<tr>
<td>Sequenced Recall {Tones [auditory]}</td>
<td>Measure of short term memory where participants hear a series of tones and then select the notes that match the tones in the order presented.</td>
</tr>
<tr>
<td>The Phone Message</td>
<td>Measure of short term memory where participants listen to an answering machine message and subsequently answer questions relating to the content of the message.</td>
</tr>
<tr>
<td>Sequenced Blocks</td>
<td>Measure of short term memory where participants first watch a hand cursor move over certain boxes and then select those boxes in the correct order.</td>
</tr>
<tr>
<td>Sequenced Words</td>
<td>Measure of short term memory where participants are shown certain words for a short duration and must select these words from a list of many.</td>
</tr>
<tr>
<td>Recognition Recall</td>
<td>Measure of short term memory where participants are shown objects for a short duration and must select these objects from a list of many.</td>
</tr>
</tbody>
</table>
Recall for Locations | Measure of short term memory where participants are shown a grid containing twelve cells in which balls are randomly positioned. Participants memorize the location of the balls so that when they are presented with an empty grid, they can insert the balls in the correct cells.

Recall for Objects and Locations | Measure of short term memory where participants are shown pictures in certain positions for a short duration and must select these objects from a display of thirty pictures.

Recall for Shapes and Places | Measure of short term memory where participants are shown a grid containing thirty cells in which shapes are randomly positioned. Participants must memorize the shapes and their locations so that when they are presented with an empty grid, they can insert the shapes in the correct cells.

Table 3: Descriptions of the PSSCogRehab memory skills exercises

<table>
<thead>
<tr>
<th>Session 1</th>
<th>Session 2</th>
<th>Session 3</th>
<th>Session 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sequenced Recall {Digits [visual]}</td>
<td>Sequenced Recall {Digits [auditory]}</td>
<td>Sequenced Blocks</td>
<td>Recall for Locations</td>
</tr>
<tr>
<td>Reversed Recall {Digits [visual]}</td>
<td>Reversed Recall {Digits [auditory]}</td>
<td>Sequenced Words</td>
<td>Recall for Objects and Locations</td>
</tr>
<tr>
<td>Sequenced Recall {Graphics [visual]}</td>
<td>Sequenced Recall {Tones [auditory]}</td>
<td>Recognition Recall</td>
<td>Recall for Shapes and Places</td>
</tr>
<tr>
<td>Colormatch</td>
<td>The Phone Message</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 4: Memory skills curriculum for second month
| **PSSCogRehab**  
| **Executive Skills**  
<table>
<thead>
<tr>
<th><strong>Exercise</strong></th>
<th><strong>Description</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Basic Concepts</td>
<td>Measure of executive functioning where participants are shown an object in the center of the screen surrounded by a several other objects and must select the surrounding object that has an attribute similar to the middle object.</td>
</tr>
<tr>
<td>Attributes and Groups</td>
<td>Measure of executive functioning where participants are shown two grids, each containing four cells that contain objects, and must move the objects so they are grouped based on their respective traits.</td>
</tr>
<tr>
<td>Flash Count</td>
<td>Measure of executive functioning where participants are shown a display of randomly placed stars for a short duration and must indicate how many stars were flashed.</td>
</tr>
<tr>
<td>Even or Odd</td>
<td>Measure of executive functioning where participants are shown a number and must quickly indicate if it is even or odd. At higher levels, participants are presented an arithmetic sequence and must add and subtract to determine if the answer is even or odd.</td>
</tr>
<tr>
<td>Digit Symbol Transfer</td>
<td>Measure of executive function where participants are shown a series of symbols and must enter the correct number for each symbol as fast as they can, according to the symbol/number pair key provided.</td>
</tr>
<tr>
<td>Sequences</td>
<td>Measure of executive function where participants are shown a display of randomly placed letters or numbers and must click on them in a certain order, as specified in the instructions.</td>
</tr>
<tr>
<td>Stroop Effects I</td>
<td>Measure of executive function where participants are shown a colored ball and two words that each spell a color. Each of the words is colored a different color from what it spells. Participants’ must select the word that spells the color of the ball as opposed to the word that is the color of the ball.</td>
</tr>
<tr>
<td>Stroop Effects II</td>
<td>Measure of executive function where participants are shown three frames and must select the bottom frame that contains the same number of numbers as the top frame.</td>
</tr>
<tr>
<td>Serial Addition</td>
<td>Measure of working memory and executive function where participants are briefly shown a number that they must add to the last number that was shown there to indicate a numerical response. Once a response is submitted, a new number flashes</td>
</tr>
</tbody>
</table>
below, which participants must add to the last number that flashed to indicate a numerical response, and so on.

<table>
<thead>
<tr>
<th>Exercise</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simultaneous Multiple Addition</td>
<td>Measure of working memory and executive function where participants are shown five numbers, one at a time, and must add them as each new number is presented to indicate a final numerical response.</td>
</tr>
<tr>
<td>Dials</td>
<td>Measure of executive function where participants are presented with dials, each of which is numbered and has a white and a red zone as well as a moving needle. Participants’ task is to keep needles out of the red zone by switching between dials and controlling needles’ directions using left and right arrow keys.</td>
</tr>
<tr>
<td>Keeping Track</td>
<td>Measure of executive function where participants are shown several balls and must track one to three of them (depending on difficulty level) as all the balls move around the screen. When the balls stop moving, participants must select the ball(s) that they were instructed to follow.</td>
</tr>
<tr>
<td>Mirror Image</td>
<td>Measure of executive function where participants are presented with a grid that is cut in half and has some of its cells filled in. Participants must fill in cells on the empty side of the grid so that it mirrors the opposite side.</td>
</tr>
<tr>
<td>Color Wheels</td>
<td>Measure of executive function where participants are shown a target color pattern model that they must reproduce by using arrow keys to rotate shapes.</td>
</tr>
</tbody>
</table>

Table 5: Descriptions of the PSSCogRehab executive skills exercises

<table>
<thead>
<tr>
<th>Session 1</th>
<th>Session 2</th>
<th>Session 3</th>
<th>Session 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basic Concepts</td>
<td>Digit Symbol Transfer</td>
<td>Serial Addition</td>
<td>Keeping Track</td>
</tr>
<tr>
<td>Attributes and Groups</td>
<td>Sequences</td>
<td>Simultaneous Multiple Addition</td>
<td>Mirror Image</td>
</tr>
<tr>
<td>Flash Count</td>
<td>Stroop Effects I</td>
<td>Dials</td>
<td>Color Wheels</td>
</tr>
<tr>
<td>Even or Odd</td>
<td>Stroop Effects II</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 6: Executive skills curriculum for the third month
3.7.2. CogSMART

The CogSMART program was created in 2011 by Elizabeth Twamley, PhD at the University of California, San Diego and the manual, which provides a comprehensive guide to facilitating the sessions, is available for free at http://www.cogsmart.com/resources. When creating CogSMART, Dr. Twamley envisioned it to be a pragmatic, cost-effective, and engaging cognitive remediation program (Twamley et al., 2012). CogSMART teaches strategies for attention and vigilance, learning and memory, executive functioning, and prospective memory through incorporating interactive activities. In addition, by making the activities game-like, the CogSMART program is able to increase participants’ motivation and focus (Twamley et al., 2012).

This program consists of twelve sessions, each ranging between one to two hours. Sessions can be carried out either in groups or one-on-one. In terms of materials, the sessions do not require many resources apart from the facilitator and client manuals. The few outside resources that are needed are planners, a deck of cards, and a ball. Each session is the same general format. First, at-home exercises are reviewed. Second, a new skill to be taught that session is introduced including the reasons for why that skill is important. Third, the new skill is demonstrated. Fourth, participants practice the new skill. Fifth, participants discuss how they can use this new skill in their lives. Sixth, at-home exercises are assigned for completion for the following week. At-home exercises are given so that participants may practice what they covered in that week’s session. The at-home exercises are designed not only to serve as a review of the material
covered, but also as application in participants’ real-world settings (Mendella et al., 2015).

One randomized controlled trial found that administration of the CogSMART program significantly improved patients’ attention and subjective quality of life following a three-month follow-up. Moreover, it significantly improved verbal memory and negative symptoms at immediate and three-month follow-ups (Twamley et al., 2012). Apart from these supportive findings, there is also evidence supporting CogSMART’s core principles. One of these principles is client-facilitator interaction. During a CogSMART session, most of the time is spent talking about goals and techniques to reach goals, as well as working in groups. The facilitators are actively involved during these activities, which, according to a recent article, is especially important for cognitive remediation programs (Cella, Reeder, & Wykes, 2016). The reason being that facilitators provide support and encouragement. Moreover, they can personalize the session for the participants so that they better understand the concepts. CogSMART facilitators make sure to learn about the participants’ personal goals and, therefore, are able to personalize sessions and link the discussed cognitive strategies/habits to participants’ goals. This increases participants’ intrinsic motivation. For very low-functioning, symptomatic participants, this can be more useful than drill-and-practice restorative cognitive remediation, which may seem overwhelming (Cella et al., 2016). The facilitators’ active role could in part explain the reductions in negative symptoms and improvements in quality of life seen in Dr. Twamley’s 2012 study (Twamley et al., 2012). These benefits could have also been due to CogSMART’s
emphasis on metacognition and applying the skills learned during the CogSMART sessions to participants’ everyday lives (Cella, Reeder, & Wykes, 2014). In terms of neurocognitive deficits in people with schizophrenia, verbal learning and memory are often regarded as the two most impaired domains. Moreover, impairments in these two domains are strongly associated with the severity of negative symptoms (Manglam & Das, 2013). Since Elizabeth Twamley’s 2012 study demonstrated CogSMART’s efficacy for improving verbal learning and memory, this therapy might be effective for reducing negative symptoms in schizophrenia.

Three participants were randomly assigned to the CogSMART experimental condition, which entailed one group training session (one to hours per session) per week for three months. The same facilitators were used for all sessions, which were recorded using a digital audio recorder. A few of these audio files were selected at random and sent to Dr. Twamley to ensure that the sessions were conducted correctly.

3.8. Statistical Measures

All data analysis was done on IBM’s The Statistical Package for Social Science (SPSS 23.0). During statistical analyses, for all tests, an alpha level of $p \leq 0.07$ was used as the anchor point for indicating a trend, and an alpha level of $p \leq 0.05$ was used as an indication of statistical significance. To analyze between-group clinical, demographic, neurocognitive, social cognitive, and functional differences, a series of one-way analyses of variance (ANOVA) were used to calculate significance. Descriptive statistics, including means and standard deviations, were also computed.
Following baseline assessment for all participants, a one-way ANOVA was used to assess significance. Then, a two by two ANOVA was performed on neurocognitive, social cognitive, and functioning measures. Lastly, a two-tailed paired-samples t-test was used for each condition and each outcome measure to determine if there were significant performance differences, for each assessment, between baseline and follow-up. Descriptive statistics, including mean and standard deviation, were also computed.

4. Results

4.1. Demographic and Clinical Characteristics

There were no significant differences between the three different conditions in regards to demographic characteristics (see Table 7). More specifically, using a one-way ANOVA, it was observed that all conditions were comparable in regards to age (p = 0.715), education (p = 0.223), mother’s education (p = 0.422), and father’s education (p = 0.373).
In regards to clinical characteristics, there were no significant difference between the three conditions (see Table 9). Using a one-way ANOVA, it was observed that all conditions were comparable in terms of duration of illness (p = 0.225), age of onset (p = 0.366), number of hospitalizations (p = 0.675), and FSIQ (p = 0.948).
<table>
<thead>
<tr>
<th>Variable</th>
<th>PSSCogRehab (n=3) x ± SD</th>
<th>CogSMART (n=3) x ± SD</th>
<th>Wait-List Control (n=3) x ± SD</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of Illness (years)</td>
<td>19.67 ± 12.74</td>
<td>33.33 ± 16.74</td>
<td>12.67 ± 8.50</td>
<td>0.225</td>
</tr>
<tr>
<td>Age of Onset</td>
<td>24.00 ± 6.00</td>
<td>17.33 ± 1.15</td>
<td>27.00 ± 12.12</td>
<td>0.366</td>
</tr>
<tr>
<td>Number of Hospitalizations</td>
<td>20.00 ± 26.00</td>
<td>9.00 ± 3.61</td>
<td>10.67 ± 8.08</td>
<td>0.675</td>
</tr>
<tr>
<td>FSIQ</td>
<td>93.33 ± 11.37</td>
<td>90.00 ± 3.61</td>
<td>92.00 ± 18.08</td>
<td>0.948</td>
</tr>
</tbody>
</table>

*Table 9: Analysis of between-group clinical characteristics (one-way ANOVA)*

### 4.2. Baseline Performance

There were no significant differences observed between conditions for any of the assessments given during baseline testing (see Table 10). Using a one-way ANOVA to compare conditions’ performances, a p-value greater than 0.05 was seen for every assessment. In fact, the lowest p-value was 0.113, which was for the negative symptom portion of the SCI-PANSS. When interpreting these results, it is important to note that higher means indicate better scores for all assessments except for WCST (errors), SCI-PANSS positive, SCI-PANSS negative, and SCI-PANSS general.
<table>
<thead>
<tr>
<th>Assessment</th>
<th>PSSCogRehab (n=3) $\bar{x} \pm SD$</th>
<th>CogSMART (n=3) $\bar{x} \pm SD$</th>
<th>Wait-List Control (n=3) $\bar{x} \pm SD$</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HVLT</td>
<td>26.00 ± 7.94</td>
<td>24.00 ± 6.93</td>
<td>20.00 ± 0.00</td>
<td>0.509</td>
</tr>
<tr>
<td>COWAT Total Letter</td>
<td>37.00 ± 16.00</td>
<td>39.67 ± 8.62</td>
<td>34.33 ± 11.59</td>
<td>0.874</td>
</tr>
<tr>
<td>COWAT Total Category</td>
<td>32.00 ± 12.53</td>
<td>44.00 ± 1.73</td>
<td>28.33 ± 6.03</td>
<td>0.120</td>
</tr>
<tr>
<td>MIST Prospective (%)</td>
<td>25.67 ± 3.06</td>
<td>32.67 ± 43.66</td>
<td>12.33 ± 11.02</td>
<td>0.645</td>
</tr>
<tr>
<td>MIST Retrospective (%)</td>
<td>56.67 ± 41.06</td>
<td>32.00 ± 10.39</td>
<td>14.67 ± 16.26</td>
<td>0.223</td>
</tr>
<tr>
<td>Digit Span</td>
<td>6.67 ± 4.51</td>
<td>7.00 ± 1.00</td>
<td>6.00 ± 2.65</td>
<td>0.922</td>
</tr>
<tr>
<td>Letter-Number Sequencing</td>
<td>6.33 ± 2.08</td>
<td>7.00 ± 1.73</td>
<td>6.33 ± 3.06</td>
<td>0.924</td>
</tr>
<tr>
<td>Digit Coding</td>
<td>4.67 ± 3.51</td>
<td>8.67 ± 2.08</td>
<td>6.00 ± 4.36</td>
<td>0.407</td>
</tr>
<tr>
<td>WCST Errors</td>
<td>36.67 ± 27.15</td>
<td>30.33 ± 18.01</td>
<td>34.67 ± 25.01</td>
<td>0.946</td>
</tr>
<tr>
<td>WCST (Percentile)</td>
<td>39.67 ± 48.43</td>
<td>40.00 ± 32.79</td>
<td>38.67 ± 51.63</td>
<td>0.999</td>
</tr>
<tr>
<td>SES Positive</td>
<td>71.62 ± 13.05</td>
<td>65.79 ± 35.27</td>
<td>63.16 ± 35.60</td>
<td>0.940</td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Median</td>
<td>p-Value</td>
</tr>
<tr>
<td>----------------------</td>
<td>--------</td>
<td>--------</td>
<td>---------</td>
<td>---------</td>
</tr>
<tr>
<td>SES Negative</td>
<td>69.47 ± 5.57</td>
<td>74.04 ± 7.52</td>
<td>55.96 ± 37.68</td>
<td>0.615</td>
</tr>
<tr>
<td>SES Social</td>
<td>73.68 ± 3.20</td>
<td>58.77 ± 5.82</td>
<td>55.09 ± 40.74</td>
<td>0.623</td>
</tr>
<tr>
<td>SFS</td>
<td>96.00 ± 4.00</td>
<td>112.33 ± 4.73</td>
<td>105.00 ± 15.39</td>
<td>0.193</td>
</tr>
<tr>
<td>SCI-PANSS Positive</td>
<td>15.00 ± 8.19</td>
<td>13.00 ± 6.08</td>
<td>16.67 ± 5.51</td>
<td>0.804</td>
</tr>
<tr>
<td>SCI-PANSS Negative</td>
<td>18.33 ± 3.06</td>
<td>15.00 ± 2.65</td>
<td>13.00 ± 2.00</td>
<td>0.113</td>
</tr>
<tr>
<td>SCI-PANSS General</td>
<td>24.67 ± 20.21</td>
<td>32.00 ± 8.19</td>
<td>30.00 ± 12.50</td>
<td>0.816</td>
</tr>
<tr>
<td>UPSA</td>
<td>60.00 ± 13.23</td>
<td>86.67 ± 5.77</td>
<td>70.00 ± 21.79</td>
<td>0.172</td>
</tr>
<tr>
<td>TASIT</td>
<td>97.33 ± 26.76</td>
<td>94.00 ± 17.35</td>
<td>108.67 ± 29.30</td>
<td>0.763</td>
</tr>
</tbody>
</table>

**Table 10:** Analysis of between-group baseline performance (one-way ANOVA)

### 4.3. Comparing Changes Between Baseline and Follow-Up Performance

An analysis of time by group effects between baseline and follow-up for each of the outcome measures (neurocognitive and functioning) was conducted using a two by two ANOVA (see Table 11). According to the p-values obtained, there were no significant time by group effects. Given the exploratory nature of this phase of the
study, where only preliminary data is considered, further analyses were conducted looking at the individual groups’ performance difference between baseline and follow-up.

<table>
<thead>
<tr>
<th>Assessment</th>
<th>F-Value</th>
<th>Degrees of Freedom</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HVLT</td>
<td>1.47</td>
<td>2, 6</td>
<td>0.302</td>
</tr>
<tr>
<td>COWAT Total Letter</td>
<td>0.00</td>
<td>2, 6</td>
<td>0.999</td>
</tr>
<tr>
<td>COWAT Total Category</td>
<td>1.70</td>
<td>2, 6</td>
<td>0.261</td>
</tr>
<tr>
<td>Digit Span</td>
<td>1.59</td>
<td>2, 6</td>
<td>0.280</td>
</tr>
<tr>
<td>SFS</td>
<td>1.15</td>
<td>2, 6</td>
<td>0.378</td>
</tr>
</tbody>
</table>

**Table 11:** Analysis of time by group effects between baseline and follow-up (two by two ANOVA)

Analysis of follow-up performance for the three different conditions, using paired-samples t-tests, determined that, with the exception of HVLT in CogSMART and Digit Span in wait-list control, there were no significant differences between baseline and follow-up performance. Participants in the first experimental condition, the PSSCogRehab group, did not demonstrate significant performance increases (see Table 12) for HVLT (p = 0.286), COWAT Total Letter (p = 0.742), COWAT Total Category (p = 0.350), Digit Span (p = 1.000) and SFS (p = 0.641) over baseline. Figures 3-5 illustrate the nonsignificant differences between baseline and follow-up performance for the PSSCogRehab group.
<table>
<thead>
<tr>
<th>Assessment</th>
<th>Baseline (n=3) x̄ ± SD</th>
<th>Follow-Up (n=3) x̄ ± SD</th>
<th>Degrees of Freedom</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HVLT</td>
<td>26.00 ± 7.94</td>
<td>29.00 ± 7.21</td>
<td>2</td>
<td>0.286</td>
</tr>
<tr>
<td>COWAT Total Letter</td>
<td>37.00 ± 16.00</td>
<td>39.33 ± 5.86</td>
<td>2</td>
<td>0.742</td>
</tr>
<tr>
<td>COWAT Total Category</td>
<td>32.00 ± 12.53</td>
<td>23.67 ± 5.69</td>
<td>2</td>
<td>0.350</td>
</tr>
<tr>
<td>Digit Span</td>
<td>6.67 ± 4.51</td>
<td>6.67 ± 2.52</td>
<td>2</td>
<td>1.000</td>
</tr>
<tr>
<td>SFS</td>
<td>96.00 ± 4.00</td>
<td>104.67 ± 23.86</td>
<td>2</td>
<td>0.641</td>
</tr>
</tbody>
</table>

**Table 12:** Analysis of follow-up performance for PSSCogRehab condition (paired-samples t-test)

The second experimental condition, the CogSMART group, did not produce performance increases (see Table 13) on COWAT Total Letter (p = 0.739), COWAT Total Category (p = 0.085), Digit Span (p = 0.742) or SFS (p = 0.148). Significant performance improvement was observed for the HVLT (p = 0.034). Figures 3 illustrates the significant difference between baseline and follow-up performance for the HVLT as well as the nonsignificant differences for the two COWAT assessments. In addition, Figure 4 and Figure 5 illustrate the nonsignificant difference for the Digit Span and SFS, respectively.
<table>
<thead>
<tr>
<th>Assessment</th>
<th>Baseline (n=3)</th>
<th>Follow-Up (n=3)</th>
<th>Degrees of Freedom</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\bar{x} \pm SD$</td>
<td>$\bar{x} \pm SD$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HVLT</td>
<td>24.00 ± 6.93</td>
<td>34.67 ± 10.02</td>
<td>2</td>
<td>0.034*</td>
</tr>
<tr>
<td>COWAT Total Letter</td>
<td>39.67 ± 8.62</td>
<td>42.33 ± 3.51</td>
<td>2</td>
<td>0.739</td>
</tr>
<tr>
<td>COWAT Total Category</td>
<td>44.00 ± 1.73</td>
<td>53.33 ± 3.51</td>
<td>2</td>
<td>0.085</td>
</tr>
<tr>
<td>Digit Span</td>
<td>7.00 ± 1.00</td>
<td>7.33 ± 2.52</td>
<td>2</td>
<td>0.742</td>
</tr>
<tr>
<td>SFS</td>
<td>112.33 ± 4.73</td>
<td>131.67 ± 10.26</td>
<td>2</td>
<td>0.148</td>
</tr>
</tbody>
</table>

**Table 13:** Analysis of follow-up performance for CogSMART condition (paired-samples t-test) (* = p<0.05)

The third condition, the wait-list control group, did not demonstrate significant performance increases (see Table 14) for HVLT ($p = 0.198$), COWAT Total Letter ($p = 0.184$), COWAT Total Category ($p = 0.713$), and SFS ($p = 0.095$). Performance improvement was observed for Digit Span ($p = 0.035$). Figure 3 and Figure 5 illustrate the nonsignificant differences between baseline and follow-up performance for the wait-list control group. Figure 4 illustrates the significant difference observed in this group for the Digit Span.
<table>
<thead>
<tr>
<th>Assessment</th>
<th>Baseline (n=3) $\bar{x} \pm SD$</th>
<th>Follow-Up (n=3) $\bar{x} \pm SD$</th>
<th>Degrees of Freedom</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HVLT</td>
<td>20.00 ± 0.00</td>
<td>32.33 ± 11.24</td>
<td>2</td>
<td>0.198</td>
</tr>
<tr>
<td>COWAT Total Letter</td>
<td>34.33 ± 11.59</td>
<td>37.00 ± 13.89</td>
<td>2</td>
<td>0.184</td>
</tr>
<tr>
<td>COWAT Total Category</td>
<td>28.33 ± 6.03</td>
<td>32.33 ± 16.20</td>
<td>2</td>
<td>0.713</td>
</tr>
<tr>
<td>Digit Span</td>
<td>6.00 ± 2.65</td>
<td>9.00 ± 3.61</td>
<td>2</td>
<td>0.035*</td>
</tr>
<tr>
<td>SFS</td>
<td>105.00 ± 15.39</td>
<td>102.00 ± 16.70</td>
<td>2</td>
<td>0.095</td>
</tr>
</tbody>
</table>

*Table 14: Analysis of follow-up performance for wait-list control condition (paired-samples t-test) (* = p<0.05)*
Figure 3: Graph illustrating the differences between baseline and follow-up HVLT and COWAT mean standard scores for all conditions

Figure 4: Graph illustrating the differences between baseline and follow-up Digit Span mean standard scores for all conditions
Figure 5: Graph illustrating the differences between baseline and follow-up SFS scores for all conditions

5. Discussion

5.1. Evaluating the Results

5.1.1. Evaluating the PSSCogRehab Intervention

Within the context of three weeks of treatment, the PSSCogRehab intervention did not confer any performance improvements relative to the CogSMART condition or wait-list control. This could have been due to a number of reasons, but the most likely one is the short duration of the intervention. At three weeks, participants in this condition completed exercises in the attention skills curriculum only. Therefore, they did not receive restorative training for memory or executive function, which the HVLT and COWAT assess. In addition, a larger sample size is required to accurately address the efficacy of the PSSCogRehab intervention.
5.1.2. Evaluating the CogSMART Intervention

According to the paired-samples t-test, the CogSMART intervention group only demonstrated a performance improvement for one neurocognitive measure, the HVLT, a measure of verbal learning and memory. Since the CogSMART program is strategy-based with an emphasis on techniques for remembering appointments and tasks that enhance verbal memory, it is expected that individuals in this group would perform better on the HVLT. None of the other assessments given at follow-up assess this domain of cognition. While the Digit Span does assess memory, the latter portions of it target working memory. It is possible that individuals performed well on the first portion of the Digit Span, which assesses short term memory, but performed poorly on the other portions of the Digit Span, bringing their overall Digit Span score down.

When trying to determine why HVLT performance significantly improved, it is important to acknowledge that the improvement may have had less to do with the CogSMART intervention and more to do with the small sample size. For example, it is possible that the three individuals in this condition were simply more focused on the day the follow-up assessment was administered. However, if that were the case, it would be expected that significant improvements would be seen for the other neuropsychological measures, which is not the case. Upon taking a closer look at individuals’ performance at baseline and follow-up, it appears that all three individuals in this condition improved their HVLT score. This eliminates the possibility of one anomalous participant who, for whatever reason, did much better on the HVLT during follow-up while the others in the group did not improve.
Another observation for this condition is that the p-value for the COWAT Total Category assessment was 0.085, which is nonsignificant, but might suggest a trend. If so, it is possible that, with more CogSMART training or a larger sample size, the mean performance improvement for the COWAT Total Category assessment will eventually become significant. Though COWAT Total Category is a measure of category fluency, a domain of cognition (semantic memory) not directly trained in CogSMART sessions, it is possible that the cognitive skills acquired during CogSMART generalize to untrained cognitive abilities. The fact that there was one significant result and one trend observed, after just three weeks of the CogSMART intervention, from a small sample size indicates the potential efficacy of this intervention.

5.1.3. Evaluating the Wait-List Control Condition

For the treatment-as-usual wait-list control group that did not receive any training, the paired-samples t-tests did not demonstrate any significant changes in scores for nearly all assessments. The exception to this is the significant improvement on the Digit Span, a subtest of the WAIS-IV. Given that participants in this condition did not receive any training or practice with this assessment, it is puzzling that performance on this neurocognitive measure improved. One potential reason for this is that, at follow-up, participants better understood their task for this assessment. That is to say that participants received practice doing this assessment during the baseline assessment, so, when doing it for a second time, they were better at it. It is also possible that these three individuals were simply more focused on the day the follow-up
assessment was given to them. Given the small sample size, it is difficult to discern reasons for why Digit Span scores significantly improved. Upon taking a closer look at individuals’ performance at baseline and follow-up, it appears that all three individuals in this group improved their score. This rules out the possibility of one anomalous participant who, for whatever reason, did much better on the Digit Span during follow-up while the others in the group did not improve.

5.2. Evaluating the Hypothesis

The hypothesis provided pertains to the full six-month long study design (see Figure 1). This thesis examines the results from the modified study design (see Figure 2); therefore, the predictions made do not apply. The full six-month long study must be completed, with a sufficient sample size, to accurately evaluate the hypothesis. Given that both experimental groups underwent cognitive remediation therapy for a period of just three weeks, it cannot be reasonably expected that significant performance improvements in baseline and follow-up test scores would be observed.

It was predicted that no significant improvements would be seen in the treatment-as-usual wait-list control group. While this group did demonstrate a p-value of 0.035 for the Digit Span, the significance of this result is called into question because of the small sample size. It cannot assuredly be said that this alleged significant performance improvement was due to simply waiting a period of three weeks.
5.3. Limitations and Future Directions

There are several limitations to the study. First and foremost, the sample size was too small, especially since it was divided into three groups. This resulted in large standard deviations for group means, which meant that statistical analyses had low power and, hence, results were less reliable. Since the study is currently ongoing, and more participants are actively being enrolled in it, the sample size will increase, which will reduce standard deviations and increase the power of statistical analyses. In addition, as more participants are added to the treatment-as-usual wait-list control condition, it is likely that changes in Digit Span performance between baseline and follow-up will no longer be statistically significant.

Apart from the small sample size, each intervention was carried out for three weeks as opposed to the scheduled three months. This meant that participants in both experimental conditions, PSSCogRehab and CogSMART, did not receive enough interventional exposure. For example, the PSSCogRehab group only completed three quarters of the first month’s attention curriculum. The efficacy of both interventions would most accurately be determined only after both experimental groups have completed their respective interventions. It is expected that the performance difference between baseline and follow-up assessments following the full three-month intervention would yield more significant results and a larger effect size. In addition, conducting a follow-up assessment three months after interventions end would help determine whether the cognitive remediation effects conferred by the interventions are maintained. While an increased duration of intervention would improve the study’s
results, it is important to note that participants do not attend every training session for either PSSCogRehab or CogSMART. This is a limitation to the study because missing sessions affects participants’ treatment and, hence, follow-up performance.

In regards to the assessments, two of them are based on self-reports: the SES and SFS. Thus, it is possible that participants provided responses to these measures of function that are not representative of their self-efficacy of social functioning, thereby skewing the results. The issue lies in the fact that assessing these two aspects of function in an objective manner is notoriously difficult. One potential solution is implemented the Specific Level of Functioning Scale (SLOF), which relies on clinicians’ assessments of patients’ function.

Another potential limitation to the study is in regards to the CogSMART sessions. The facilitators of these sessions were psychology interns who had experience working with people with psychosis. They also received training on how to facilitate the CogSMART sessions. However, this was their first time teaching a strategy-based cognitive remediation program, so there was room for error on their part, thereby calling into question the fidelity of CogSMART administration. Though the CogSMART manual provides a comprehensive guide to facilitating sessions, it is likely that the CogSMART facilitators for this study were still not able to ensure that participants got the most out of the sessions. Recordings of the CogSMART sessions have been sent to Dr. Twamley for feedback; therefore, as the study moves forward, facilitation of the CogSMART sessions will improve.
The CogSMART manual specifies that facilitators are not to use extrinsic motivators not indicated in the manual. Therefore, participants were made to understand that they would not be paid for attending sessions. Both of the CogSMART session facilitators and other members of the RVS staff expressed that CogSMART attendance would be more consistent if participants were monetarily compensated for attendance. However, literature on the use of monetary extrinsic motivators in cognitive remediation therapies does not suggest its effectiveness. For example, one study evaluating the use of motivators in cognitive remediation for schizophrenia indicates that soft extrinsic motivators, such as points or certificates, could be better for encouraging learning compared to monetary incentives (Medalia & Saperstein, 2011). Another study on motivation in cognitive remediation suggests that soft extrinsic motivators can be effective for very cognitively impaired participants with low intrinsic motivation (Silverstein, 2010), which accurately describes the sample population of the study at hand. During CogSMART sessions, participants responded well to soft motivators, namely praise and other positive reinforcement. Therefore, a future direction for this group is to create a point system to further encourage participants’ attendance.

One of the strengths of the study is that, at baseline, none of the groups differed significantly on demographic and clinical characteristics, which suggests that the results obtained for neuropsychological assessments were not due to the confounding effects of baseline test performance differences between groups.
5.4. Conclusion

In summary, the restorative PSSCogRehab and strategy-based CogSMART interventions did not produce differential effects on neurocognitive and functioning measures in this limited duration clinical trial. They also did not show superiority over a treatment-as-usual wait-list control group. Individual group analyses revealed improvement in the HVLT in the strategy-based CogSMART condition, and improvement in the Digit Span in the treatment-as-usual wait-list control. The small number of subjects and high number of comparisons could suggest that these significant findings may reflect type I error.
6. References


https://doi.org/10.1093/schbul/sbr084

https://doi.org/10.1016/S0140-6736(78)91740-3


https://doi.org/10.1375/brim.10.1.23

https://doi.org/10.1038/nature13595


https://doi.org/10.1093/schbul/sbs092


Appendix

Appendix A: Informed Consent

Submitted: 12/23/16

RIVER VALLEY SERVICES /DEPARTMENT OF MENTAL HEALTH AND ADDICTION SERVICES (DMHAS)
INFORMED CONSENT FOR PARTICIPATION IN RESEARCH

PRINCIPAL INVESTIGATOR: Matthew M. Kurtz
DEPARTMENT: Psychology
PHONE: 860-685-2072
EXPECTED DURATION: Five years
SPONSOR: Wesleyan University

I. You have been asked to participate as a participant in the research study, “Comparing the Efficacy of Two Forms of Cognitive Remediation: Strategy-Based vs. Drill-and-Practice Restoration Training for Cognitive Deficits in People with Psychosis,” because you have been diagnosed with schizophrenia, schizoaffective disorder, or some other mental health disorder involving psychosis. Drill-and-practice restoration cognitive remediation training is an intervention consisting of a series of computerized attention, memory and problem-solving exercises that you practice on and that are designed to improve your concentration skills. Strategy-based cognitive remediation training consists of a series of weekly meetings in which you are coached to develop skills in using calendars, notebooks, and other memory support tools to help you work around any difficulties you may have in your attention and memory.

In order to decide whether or not you wish to be part of this research study you should know enough about its risks and benefits to make an informed judgment. This consent form gives you detailed information about the research study, which a member of the research team will discuss with you. This discussion should go over all aspects of this research: its purpose, the procedures that will be performed, any risks of the procedures, possible benefits and possible alternative treatments. Once you understand the study, you will be asked if you wish to participate; if so, you will be asked to sign this form.

The purpose, procedures, and length of your involvement are stated below:

**A. Purpose of research:** To compare the efficacy of two different forms of cognitive remediation for people with schizophrenia.

**B. Procedures:** Your participation in this study will involve the following procedures:
1. You will be asked to answer questions about your education, illness, medications and complete a series of neuropsychological assessments before and after your treatment and 3-months after the cessation of cognitive remediation groups. These tests will take a couple of hours and are in addition to your standard clinical care. These tests will help tell us determine whether your treatment has worked and which form of cognitive skills training is more effective at improving your cognition.

2. You will be assigned, by chance, to one of three groups: a strategy-based training group, a drill-and-practice training group or a wait-list control group.
   - For the wait-list control group, you will be assigned to either the strategy-based training group or the drill-and-practice training group following a period of three months.
   - If assigned to the strategy-based training group, you will practice cognitive (thinking) exercises one to two hours a day, once a week. This training will occur over a 3-month period.
   - If assigned to the drill-and-practice training group, you will practice cognitive exercises two hours a day, three times per week. This training will also occur over a 3-month period.

You should know that data we collect in this project will likely be used for comparison to data from other studies in our center or in cooperation with other researchers. Any data used in this manner will be stripped of information that would identify whom it came from.

You should also know that you will be requested to sign a separate release-of-information form. If you sign this form you will give the researchers conducting this study access to review your hospital records. Information regarding your past and present medical history will be gathered from these files.

You may be asked to be video or audiotaped while completing some of the neuropsychological assessments or clinical treatment groups such as strategy-based training or drill-and-practice training. Confidentiality regarding video or audiotapes will be protected by the researchers running this study. More specifically, media will not be labeled with your name, will be kept in a locked file in the Principal Investigator’s lab suite at Wesleyan University and will be viewed only by staff directly involved in the research study. Recordings will be kept for a maximum of five years after collection.

We will ask whether you want to release information collected as part of this research study to your treatment team at River Valley Services. If so, we will ask you to sign a release-of-information form.
You may decide that you do not want to complete some portion of the cognitive testing and illness assessment that occurs before and after your computer training and still participate in the study.

C. Duration of Participation: This study will take place at River Valley Services Connecticut Valley and your participation in the cognitive remediation training will last for approximately 3 months.

II. The possible risks, discomforts and side effects of the procedures are described below, including what we will do to minimize risk:

1. You may become fatigued or mildly anxious during the interviews and testing. You are free to take breaks at any time. Some of the interview questions may touch on sensitive topics. You are free to skip a question if you feel uncomfortable answering it.

2. You may experience mild anxiety using a personal computer.

3. You may become mildly tired from the cognitive exercises and social skills training.

4. You may experience a feeling of mild discomfort while being video or audiotaped.

5. A breach of confidentiality could occur. Nonetheless, your confidentiality will be protected to the greatest extent possible. Your records will be maintained in accordance with applicable state and federal laws.

III. There are possible benefits to you or others to be expected from your participation in this research as described below:

1. By your participation, you may provide information that will benefit future patients with the same difficulties that you experience.

2. Individual benefits, however, cannot be guaranteed.

IV. There may be other treatments for your condition. You should consider these as well as the treatments in the study just described. Whether you choose to participate or not you will receive your usual care at River Valley Services.

V. The investigator is willing to answer any questions you may have concerning the procedures herein described. You do not have to sign this consent until all the
questions you have at this time have been answered. Future questions about this study may be directed to Dr. Matthew Kurtz at (860) 685-2072.

If you have any confidential issues to discuss, such as problems or complaints, you may call Janet Storey, DMHAS IRB Chair, (860) 418-6823, who is not part of the research.

VI. Your participation is voluntary and you may refuse to participate and/or withdraw your consent and discontinue participation in the project at any time without penalty or loss of benefits to which you are otherwise entitled. Your decision whether or not to participate will not affect your future medical care at River Valley Services.

You will receive financial compensation as discussed below. If you receive compensation, it will be reported as income to the Internal Revenue Service (IRS) if you receive $600 or more in a year for research studies completed through River Valley Services.

You will be paid $30 for completion of the questions about your medical history and baseline neuropsychological assessments at entry to the study, another $30 for completion of these same questions and tests at the end of your cognitive remediation training, approximately 3 months after entry to the study and then a third time three months after the cessation of your cognitive remediation training. These payments may be reported to the federal government for tax purposes. The payments will be issued via gift cards and will be given to you directly upon completion of each portion of the study.

There is no financial cost to you for participating in the study.

VII. Your confidentiality will be protected to the greatest extent possible. River Valley Services will protect all the information about you and your part in this study just as is done for all patients at River Valley Services. Your records will be maintained in accordance with applicable state and federal laws. However, private identifiable information about you may be used or disclosed for purposes of this research project. You may request that your records be released to your personal physician.

The information that may be used or disclosed includes the following:

1. Results of tests of attention, memory and problem-solving.
2. Results of tests of your functioning in the community, e.g., ability to plan trips, plan a meal, socialize, etc.
3. The interview we conduct to for measurement of your specific symptoms related to having schizophrenia or schizoaffective disorder or another psychiatric disorder.
4. Age, race and gender.
5. Medical and psychiatric history.
6. Records of your progress in cognitive remediation.

**This information may be used or disclosed by:**
1. Dr. Matthew M. Kurtz and clinical research staff working under his direct supervision.
2. My treatment team at River Valley Services.

**The information may be disclosed to:**
3. DMHAS and/or Wesleyan University Institutional Review Board.

**The purpose(s) of the use or disclosure of this information is (are):**
4. To answer the research question.
5. To ensure the study is being conducted properly and that your rights as a participant are protected.

**The use or disclosure of the information is permitted until:**
Completion of the research study.

By signing this consent, you are also agreeing to the use or disclosure of your protected health information as described above. If you do not agree to the use or disclosure of the information as described and therefore do not sign this consent, you will not be in the study.

If, after signing the consent, you change your mind, you have the right to revoke your consent, in writing. However, you will be withdrawn from the study. If you have completed 5 or less hours of skills training your data will not be included in the study. If you have completed more than 5 hours of skills training, your data will be included in the study unless you notify us that you do not want your data included. If you withdraw your consent you will not be able to continue computer training. Regardless of your participation or lack of participation, the rest of your treatment at River Valley Services will not be affected in any way.

**VIII.** In case of any injuries as a direct result of taking part in this research project, you will receive help in the following way:

If you have medical insurance, River Valley Services will collect fees for medical treatment from your insurance company. RVS will not pay medical expenses at other hospitals or pay for pain and suffering, travel, lost wages, or other indirect costs of taking part in this project.
IX. Signatures

I hereby voluntarily agree to participate in the research study entitled, “Comparing the Efficacy of Two Forms of Cognitive Remediation: Strategy-Based vs. Drill-and-Practice Restoration Training for Cognitive Deficits in People with Psychosis,” described in this consent form.

You will be given a signed copy of this informed consent form to keep.

_________________________________________  
Participant's Signature // Date

_________________________________________  
Conservator Signature and Relationship to Participant// Date

_________________________________________  
Investigator’s Signature or Person Obtaining Consent // Date

_________________________________________  
Witness (person observing the explanation of the above information to the participant) - optional unless consent is presented orally.

I voluntarily agree to have my answers to questions about my illness video and/or audiotaped.

_________________________________________  
Participant's Signature // Date

_________________________________________  
Conservator Signature and Relationship to Participant// Date

_________________________________________  
Investigator’s Signature or Person Obtaining Consent // Date

_________________________________________  
Witness (person observing the explanation of the above information to the participant) - optional unless consent is presented orally.
Appendix B: RVS Release of Information Form

STATE OF CONNECTICUT
DEPARTMENT OF MENTAL HEALTH AND ADDICTION SERVICES
RIVER VALLEY SERVICES
P.O. Box 351 – Middletown, Connecticut 06457
Telephone: 800-262-5209      Fax: 860-262-5339

AUTHORIZATION FOR USE AND DISCLOSURE OF PROTECTED HEALTH INFORMATION
THIS IS A LEGAL DOCUMENT AND WILL NOT BE HONORED UNLESS IT IS COMPLETED IN FULL

Patient/Client (Last Name, First Name)          Date of Birth          MPI #          Last 4 digits of SS#
I, the undersigned, authorize the above named facility to: □ DISCLOSE information to □ OBTAIN information from
Name of Person ___________________________________________ Name of Organization ________________________________
Address: _____________________________________________________________
City ___________________________ State ___________ Zip Code ___________
I understand that this authorization is voluntary and that information to be released/obtained may include Medical, Psychiatric, Substance Abuse and/or HIV/AIDS treatment information unless otherwise specified:
Limitations/Restrictions
Purpose of Release: □ Evaluation/Treatment □ Benefit Determination
□ Placement/Referral □ Case Management Coordination
☐ Research study

Information to be released/obtained: (Check Appropriate Boxes)
☐ Psychiatric Evaluation ☐ Medical History and Physical Exam ☑ Diagnostic Reports (specify):
☐ Psychosocial History/Assessment ☐ Discharge/Transfer Summary
☐ Psychological Evaluation ☐ Medication Records
☐ Treatment Plans ☐ Other (specify):

Dates of Treatment Covered by this Request:
☑ All prior episodes of care, through discharge from present episode of care
□ Limited to the following Dates(s):
This authorization, if not cancelled, will expire:
Date (not to exceed 12 months), event or condition upon which this authorization expires.
If blank, authorization will expire 12 months from date of signature below.

I understand that refusal to sign this authorization form will in no way affect my right to obtain present and future treatment, except where disclosure of such communications and records is necessary for treatment. I also understand that I may revoke this authorization at any time by signing the “CANCELLATION/REVOCATION” section below, except to the extent that action has been taken in reliance on it. I further understand that the confidentiality of psychiatric, substance abuse and HIV/AIDS records are protected under State and Federal Laws and cannot be disclosed without my written authorization unless otherwise provided for by law. The information disclosed by this facility pursuant to this authorization may be subject to re-disclosure by the recipient and no longer protected by Federal law. I understand that this authorization is voluntary and that information to be released/obtained may include Medical, Psychiatric, Substance Abuse and/or HIV/AIDS treatment information unless otherwise specified above.

Signature of Patient/Client/Authorized (Legal) Representative* Date
A copy of this authorization will be provided to the Patient/Client/Authorized Representative as requested.

CANCELLATION/REVOCATION:
Signature of Patient/Client/Authorized (Legal) Representative* Date
*If this form has been signed by the patient’s/client’s Authorized (Legal) Representative, a copy of the legal appointment must be attached: ☐ Conservator/Guardian ☐ Executor of Estate ☐ Other (specify):

Office Use Only: ☐ File only ☐ Send attention to:

NOTE: Confidentiality of psychiatric, drug and/or alcohol abuse and HIV records is required and no information from these specific records shall be transmitted to anyone else without written consent or authorization as provided under Connecticut General Statutes, Chapters 99c and 368x and Federal Regulations 42 CFR 2. These laws prohibit you from making any further disclosure without specific written consent of the person to whom it pertains. A general authorization for the release of information is NOT sufficient for this purpose.

Revised: 4/1/10          DMHAS form #100-RVS

83
Appendix C: HIPAA Release Form

AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION FOR RESEARCH PURPOSES

The federal privacy law, Health Insurance Portability & Accountability Act (HIPAA), protects your individually identifiable health information from being shared without your permission. The privacy law requires that you sign an authorization (or agreement) in order for researchers to be able to use and disclose your protected health information and that you receive a copy of the Institution’s privacy practices.

Your signature on this authorization is voluntary. Whether you choose to sign or not to sign has no impact on your treatment, payment, or enrollment in any health plans, or affect on your eligibility for benefits. The only consequence of not signing this form is that you may not be allowed to participate in this research project.

By signing this form you authorize Dr. Matthew Kurtz and his staff to use and disclose your protected health information for the research project titled “Cognitive Remediation for Schizophrenia: Effects on Distal Outcome Measures and Relationship to Social-Skills Training”. You also permit your doctors and other health care providers to disclose your protected health information for this research project.

In addition, State of Connecticut statutes require that any release of information pertaining to AIDS, HIV infection, behavioral health services, psychiatric care, or treatment for alcohol and/or drug abuse be specifically authorized. If this information pertains to you, you should know that the researcher(s) and staff associated with this project might become aware of it. By signing this dual-purpose authorization you acknowledge that you understand there is a chance this information may be subject to use and disclosure as it relates to this project.

This Authorization does not have an expiration date. However, if you sign this authorization you can still change your mind at a later date. You can revoke this authorization by sending a written notice to Dr. Matthew Kurtz, Department of Psychology, Wesleyan University, Middletown, CT. 06459, to inform him of your decision. Once you revoke this authorization the researchers will no longer be able to use and disclose your protected health information. There are exceptions to this. For example, one exception under which the researchers may continue to use and disclose your protected health information after receiving your request to revoke the authorization is if you experience(d) an adverse event (bad effect). Another example is that researchers may continue to use and disclose only the protected health information collected for the research study prior to receiving the request to revoke
this authorization. If you revoke this authorization you may no longer be allowed to participate in this study.

If you have any questions, concerns or complaints about your privacy rights, you may write to the Federal Department of Health and Human Services (DHHS) at DHHS Regional Manager, Office of Civil Rights, U.S. Dept. of Health and Human Services Government Center, J.F. Kennedy Federal Building, Room 1875, Boston MA 02203. Complaints should be sent within 180 days of when you knew, or should have known, of the problem.

You may not be allowed to review the information collected for this research project until the study is complete. However, you have the right to request that your medical record be released to your personal physician. When the collection of information is complete, you may have the right to access all of your information.

Your protected health information that may be used and disclosed includes:

- Race, gender, age
- Neuropsychological test data, functional and social skill measurements, and symptom rating data
- Medical and psychiatric history
- The interview we conduct to confirm your psychiatric diagnosis and measurement of your specific symptoms related to having schizophrenia or schizoaffective disorder.
- Records of your progress in cognitive remediation and social skills training.

Your Health Information will be used to:

- To answer the research question.
- To ensure the study is being conducted properly and that your rights as a participant are protected.

Your Protected Health Information may be used by and shared with:

- The Hartford Hospital and/or DMHAS Institutional Review Board.
- The National Alliance for Research in Schizophrenia and Depression (NARSAD).
- The Department of Psychiatry at Dartmouth Medical School.

The researchers and staff agree to protect your health information by using and disclosing it only as permitted by you in this Authorization, as directed by state and federal law. However, once your health information has been disclosed to anyone
outside of this institution, the information may no longer be protected under this authorization.

There may be studies conducted in the future for which you may be an eligible participant. Please initial your preference.

_____ You give permission to Dr. Matthew Kurtz or his designated administrator to contact you with information about future studies for which you may be an eligible participant.

_____ You do not give permission to be contacted about future studies for which you may be an eligible participant.

You are a voluntary participant in this research study, or you are authorized to act on behalf of the participant. By signing you acknowledge that you have read and understand this form and that you authorize the use and disclosure of protected health information. You will receive a copy of this form after it is signed.

Signature of the research participant or the research participant’s legal representative*.  

Date

Printed name of the research participant and if applicable the participant’s legal representative*

Representative’s relationship to the research subject

*Please provide documentation of your status as an authorized representative
Appendix D: RVS Clinical Director Request for Approval

STATE OF CONNECTICUT
DEPARTMENT OF MENTAL HEALTH AND ADDICTION SERVICES
RIVER VALLEY SERVICES

DATE: November 9, 2016
TO: IRB
FROM: Michelle Leister, LCSW
Clinical Director, River Valley Services
RE.: Research Project with Dr. Kurtz

RVS would fully accept Dr. Kurtz’s proposal for conducting research on cognitive remediation at this facility with the approval of the Institutional Review Board.

Celeste Cremin-Endes, CEO, Michelle Leister, Clinical Director and Dr. Margaret Meskell, Supervising Psychologist have reviewed the research conditions. The components of the research project include random assignment to two kinds of treatment; one computer based and one group and pre and post neuropsychological assessment for participants in which they will be paid a stipend for their time ($30.00) per assessment.

In my role as Clinical Director of RVS, I feel confident that the risk of harm to clients is minimized, while the opportunity for benefit is potentially high. Participation in this study will impact the weekly structure of our clients in a positive way, and is expected to help them with key functional and social skills that would allow them to manage their illness better.

I request approval for this project.

Sincerely yours,

Michelle Leister, LCSW
Clinical Director

Phone: (860) 262-5200  Fax: (860) 262-5290
P.O. Box 351 • Silver Street, Middletown, CT 06457
An Equal Opportunity Employer
Appendix E: DMHAS Commissioner Approval

STATE OF CONNECTICUT
DEPARTMENT OF MENTAL HEALTH AND ADDICTION SERVICES
A Healthcare Service Agency

DANIEL P. MALLOY
GOVERNOR

MIRIAM E. DELPHIN-RITTMON, Ph.D.
COMMISSIONER

January 26, 2017

Celeste Cremin-Endes, LCSW, MPH
Chief Executive Officer
River Valley Services
P.O. Box 351
Middletown, CT 06457

Re: Comparing the Efficacy of Two Forms of Cognitive Remediation: Strategy-Based vs. Drill-and-Practice Restorative Training for Cognitive Deficits in People with Psychosis

Dear Ms. Cremin-Endes:

The proposed study, “Comparing the Efficacy of Two Forms of Cognitive Remediation: Strategy-Based vs. Drill-and-Practice Restorative Training for Cognitive Deficits in People with Psychosis” submitted by Matthew Kurtz, Ph.D., has been reviewed by the Office of the Commissioner. It has been determined that this project has scientific merit and that information gained would be of potential usefulness to DMHAS. The project is approved, and I send my best wishes for a successful research project.

Thank you.

Sincerely,

Miriam E. Delphin-Rittmon, Ph.D.
Commissioner

cc: Eleni Rodis, M.S.
    Janet Storey, MSW
# Appendix F: DMHAS IRB Chair Approval

## STATE OF CONNECTICUT

**DEPARTMENT OF MENTAL HEALTH AND ADDICTION SERVICES**

_A Healthcare Service Agency_

---

### NOTICE OF INITIAL IRB APPROVAL

_February 17, 2017_

**Title of Study:** Comparing the Efficacy of Two Forms of Cognitive Remediation: Strategy-Based vs. Drill-and-Practice Restorative Training for Cognitive Deficits in People with Psychosis

**Principal Investigator:** Matthew M. Kurtz, PhD, Professor of Psychology

**Reference Number:** 16-13

**Type of Review:** Expedited

**Approval Date:** 02-27-17

**Approval Expiration Date:** 02-27-18

---

**Dear Dr. Kurtz:**

Your study, referenced above, has received approval by the DMHAS Institutional Review Board. IRB approval is valid through February 27, 2018.

Your study was eligible for expedited review under Category 7. The study must be re-approved in order for research activities to continue beyond the above noted expiration date. An Application for Continued Approval must be submitted at least 30 calendar days prior to the approval expiration date; a blank application is attached. You will be contacted regarding the date of the continuation review.

If any changes are contemplated following the date of this approval, a written request outlining the proposed changes must be submitted to the IRB for review and approval before implementation. No changes to the approved protocol or informed consent may be made without IRB approval.

The IRB should be informed, as outlined in the DMHAS IRB Policy and the DMHAS IRB Guidelines for Investigators, of any adverse events, protocol deviations, complaints or other unanticipated problem involving risks to research participants related to your study. The IRB Policy, Guidelines

---

(860) 418-7000
410 Capitol Avenue | P. O. Box 34131 | Hartford CT 06114
www.ct.gov/dmhas
An Equal Opportunity Employer
Notice of DMHAS OOC IRB Approval

for investigators and related IRB information may be accessed at the DMHAS web page

If you have any questions, please feel free to contact me at (860) 418-6823.

Sincerely,

[Signature]

Janet Storey, M.S.W.
Chair, Institutional Review Board