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COMPUTER-BASED BRIEF MOTIVATIONAL INTERVENTION FOR MEDICATION ADHERENCE IN SCHIZOPHRENIA

by

ROBERT G. KENDER

DISSERTATION

Submitted to the Graduate School

of Wayne State University,

Detroit, Michigan

in fulfillment of the requirements

for the degree of

DOCTOR OF PHILOSOPHY

2010

MAJOR: PSYCHOLOGY (Clinical)

Approved by:

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Advisor Date

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DEDICATION

I want to dedicate this work to all of those who have gone before me, all who are no longer here, yet who affect me profoundly each and every day of my life. However, this dedication is especially for two people who I miss dearly. The first is Donald Glenn Kender. I want to dedicate this to you, dad. Your son is now a doctor. After you left, I finally kept my promise…well, almost. It took just over another 2 years.

And finally, for Candace Marie Bolter, and he who never was. I truly hope that you are together now, and part of me is with you, just as you will always be with me. I love you.

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There are so many people who have been with me on this journey, and I know that I will never be able to remember each and every one that deserves to be listed here. However, there are a few that I feel that I have to mention for their invaluable assistance. I truly do love you all.

My parents, Donald and Bonnie Kender who, with my "aunt" Darlene Goode fed me all the knowledge I could handle growing up. "Doc" Robert Charles Cronin, Ph.D. for telling me that of course I could go to college, and similarly, Charles E. M. Dunlop, Ph.D. for telling me that of course I could go to graduate school (although I know that Philosophy was our original idea…sorry Chuck, but the field is better off as it is). I should probably mention Amanda Osborne, without whom I would have never even finished the application process. I need to thank Stefanie Tweedly, even though you almost beat me to the finish. I would like to also thank Nancy Lockhart for her support under fire, and of course, Phebe Lam, **Ph.D.** for continuously reminding me that failure and surrender are not options. I also cannot forget Cheryl Dahle for coming through in the clutch. Thanks for that. I want to thank Paul Lucki Smith, for dangling the carrot mercilessly.

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And Candace. Always Candace.

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CHAPTER 1

INTRODUCTION

The following study is a randomized clinical trial designed to examine the effects of a computer-delivered form of motivational interviewing on medication adherence in individuals suffering from schizophrenia. First, however, I will review the history and background of this disorder, the importance of medication in its treatment, and ways that treatment adherence have and can be addressed.

Schizophrenia in society

Schizophrenic disorders are devastating for most people who are afflicted, and very costly for family and society. The onset of a schizophrenic disorder generally occurs in the late teens to mid twenties, with some significant symptoms typically showing in early childhood. If inadequately treated, a person with a schizophrenic disorder is likely to experience a chronic course of the illness resulting in severe functional impairment in many major life domains (Fenton & McGlashan, 1992; Hollis, 2000; McClellan, McCurry, Speltz, & Jones, 2002; Robinson, Woerner, Alvir, et al., 1999). Untreated persons often become unproductive members of society, dependent on family and public health as well as mental health resources (with overall annual nation-wide direct costs estimated at $62.7 billion) (Wu, et al., 2005).

This introduction will briefly examine the history of the classification of the disorder itself, its course, and some of the major theories of causation. Subsequent sections will review treatment approaches and the key issue of adherence to treatment.

History

Hindu elders wrote descriptions matching those of schizophrenia in the Ayur-veda over 3400 years ago. A systematic review of Greek and Roman literature from the 5th century B.C. through the 2nd century A.D. reveals that the peoples of these civilizations recognized a number of psychological and even psychotic symptoms, even though there does not seem to be evidence that a syndrome matching the criteria for modern-day schizophrenia was delineated (Evans, McGrath & Milns, 2003).

The notion that mental illness possesses a genetic or hereditary component is more recent. Battie (1758) saw that his patients had lunatic ancestors and Esquirol (1838) asserted that “heredity is the commonest cause of insanity” (Shorter, 1997). By the time Kraepelin adopted Morel’s (1857) theory of degeneration for the fourth edition of his textbook, the term dementia praecox was steadily evolving into the concept of schizophrenia that we know today (Ban, 2004). This new term was coined by Bleuler, who characterized the syndrome by placing emphasis on four A’s: loose Associations, inappropriate Affect, Ambivalence, and Autism. These four symptoms dominated the diagnostic criteria until Schneider (1957) postulated the first-rank symptoms (FRS) of audible thoughts, voices arguing/talking/commenting, somatic passivity experiences, thought withdrawal/broadcasting, delusional perceptions and experiences of mad volition, affect and impulse. Mellor (1982) later found that FRS are not exclusive to schizophrenia.

While there have been other influential classification parameters suggested for schizophrenia (e.g., Kleist, 1960; Leonhard, 1957), it is interesting to note that none of them are a major part of today's DSM-IV criteria. Although Schneider's FRS are present to some degree in the diagnostic criteria of the ICD-10, the DSM-IV focuses predominantly on patient's experiencing hallucinations, delusions, disorganized behavior and speech, and the negative symptoms of avolition, alogia and affective flattening (Andreasen, 1983).

Course

Schizophrenia has been described as following a relatively predictable four-phase course. In the first or pre-morbid phase, subtle cognitive and social difficulties begin to surface. This is followed by a prodromal phase. This second phase is characterized by a gradual emergence of "subtle psychotic-like symptoms, social withdrawal and functional decline." The third, or psychotic phase often includes florid hallucinations or delusions, while the transitional (also called "recovery") phase marks the return to prior levels of functioning (although individuals are now more prone to relapse). Finally, there is a stable or residual phase that is free from the psychotic aspects of the disorder but includes persistent deficits in both cognitive and social functioning (Keshavan, 2005).

Conceptual models of causation

A. Environmental Factors

It is clear that the development of schizophrenia is not solely based on genetic inheritance; for example, concordance for monozygotic twins is 35-50% rather than 100%. One of the most enduring conceptualizations of the etiological

development of schizophrenia is what has come to be called the diathesis-stress model, which began with Paul Meehl's landmark paper suggesting that the expression of schizophrenia is a function of a congenital predisposition (of varying strength) and environmental factors such as positive or negative "social reinforcement regimes," with certain minimal levels of each being necessary for the disorder to manifest (Meehl, 1962). He further postulated that other inheritable factors such as resistance to stress and physical vigor could be protective. This idea was greatly expanded over a decade later by Zubin and Spring, who focused predominantly on the vulnerability aspect of the disorder (Zubin & Spring, 1977). Although their model is far too complex to recreate in detail, it is important to note that there was a great deal of emphasis placed on not only environmental contingencies, but on coping strategies as well. Individuals were seen as having a genetic vulnerability to schizophrenia that was impacted by environmental forces, social-psychological experiences, and other genetic predispositions that may leave them more or less susceptible to stress, as well as protective factors such as social support and personal coping strategies and skills.

Recent studies have supported the diathesis-stress model. For example, Howes et al. point out that even though schizophrenia is heritable, it is not caused by the inheritance of a single gene, just as medical disorders such as coronary artery disease and diabetes are not the result of an identified single gene (Howes, McDonald, Cannon, Arseneault, Boydell and Murray, 2004). There are at least two genes that have been implicated; neuregulin for

neurodevelopmental problems (Stefansson, Steinthorsdottir, Thorgeirsson, Gulcher and Stefansson, 2004) and COMT (catechol-O-methyltransferase) for problems with dopamine regulation (Shifman, Bronstein, Pisante-Shalom, Lev-Lehman, Weizman, et al., 2002). Furthermore, many environmental factors continue to impact the likelihood that an individual will develop a schizophrenia-spectrum disorder, including obstetric complications, stress, drug use, immigration, season of birth, head injury, and viral infection (for a complete review see, Austin, 2005).

B. Biological Factors

Recent conceptual models seek to explain the underlying brain mechanisms responsible for schizophrenia, and focus on very specific etiological sequale. The early developmental model posits perinatal abnormalities in brain development as the mediating factor for problems in brain functioning in early adulthood (Murray & Lewis, 1987; Weinberger, 1987). There are data that support this theory, in that there is a higher rate of birth complications, minor physical defects, behavioral problems, and neurological soft signs in children who later develop schizophrenia, but only a small percentage of those who exhibit these early difficulties actually develop schizophrenia (Keshavan, 2005).

Because schizophrenia develops in late adolescence/early adulthood, another theory postulates that the disease is the result of normal developmental processes gone awry. Specifically, during this period there is normally a “pruning” of surplus synapses that, if excessive, could lead to a reduction of synapses that may lead to the onset of the disorder (Feinberg, 1982; Feinberg,

1990; Keshavan, et al., 1994). Others (e.g., Lieberman et al., 2001) have observed that many patients deteriorate during the first few years after the onset of the illness, which suggests that a degenerative process may be at work.

The pathophysiological models described above need not be mutually exclusive and may even occur in a sequential manner. As stated by Lieberman, "…etiologic and pathogenic factors occurring long before the formal onset of the illness (probably in gestation) disrupt the course of normal neural development, resulting in subtle alteration of specific neurons and circuits, which confer vulnerability and may ultimately lead to malfunction", (Lieberman et al., 2001). This view is shared by others (e.g., Bloom 1993; Lewis & Lieberman 2000; Murray & Lewis 1987; Weinberger 1987). This may be compounded or facilitated by environmental factors (see earlier section), as illicit drug use and stress have been identified as having a contributory impact on the disorder.

Brain changes: structural and chemical.

There is substantial evidence that persons diagnosed with schizophrenia show characteristic differences in brain structure. Specifically, increased lateral ventricle, reduced overall brain volume, reduced bilateral temporal lobe (Lawrie & Abukmeil, 1998), reduced size of the corpus callosum (Woodruff, McManus & David, 1995) and reduced hippocampus and amygdala-hippocampal complex sizes have all been reported. More recently, Wright and colleagues confirmed association with increased ventricle volume and reduced overall cerebral volume as well as increased basal ganglia structures and bilateral medial temporal lobes (Wright, et al., 2000).

There is also evidence of chemical differences in the brains of individuals suffering from schizophrenic disorders. In a comprehensive historical review of factors leading to what is now known as “the dopamine hypothesis,” Baumeister (2002) suggests that the discovery of reserpine, a drug derived from a sub-Himalayan shrub and used originally as a psychiatric sedative, was the starting point for this research. Named as a “tranquilizer” in 1953, it later became one of the first drugs included in neuroleptics, or drugs with extrapyramidal side effects (Bein, 1970; Deniker, 1983). During this same time, serotonin was also being studied. Its connection to mental disorders was discovered by Gaddum, who observed that it antagonized LSD and determined that it therefore plays a role in maintaining sanity, and also by Woolley and Shaw, who noted that a lack of serotonin, or administration of serotonin antagonists, produces “mental aberrations” similar to those found in schizophrenic individuals (Gaddum, 1954; Woolley & Shaw, 1954).

While the previous research is important for the current understanding of the neurotransmitters involved in schizophrenia, research into the mechanisms of action for stimulants is most responsible for the formation of the dopamine hypothesis. Jacques van Rossum, studying the action of amphetamines, found that they activated dopaminergic receptors and that these receptors are responsible for the psychomotor effects of stimulants (Rossum, 1963, 1964). Combined with the fact that extrapyramidal motor disturbances were known to be mediated by dopaminergic mechanisms and neuroleptics produce these disturbances, van Rossum concluded, “When the hypothesis of dopamine

blockade by neuroleptic agents can be further substantiated it may have fargoing consequences for the pathophysiology of schizophrenia. Overstimulation of dopamine receptors could then be part of the aetiology. Obviously, such an overstimulation might be caused by overproduction of dopamine, production of substances with dopamine actions (methoxy derivatives), abnormal susceptibility of the receptors, etc." (Rossum, 1966, 115-126).

The importance of the previous section cannot be overstated, as it has a direct relevance to the drugs used to treat schizophrenia today. Even though it clearly does not tell the entire story of the neurological underpinnings of schizophrenia, it has helped to guide research on pharmacological interventions. To date, these are the most effective means available for treating schizophrenic disorders and there is some evidence that continuous medication is required to avoid relapse (Kane, 1996); multiple relapses can result in a progressive deterioration of mental functioning in some patients and leave them unable to regain their previous level of functioning (Johnson, 1983).

Pharmacological interventions

There are a number of medications currently available to individuals suffering from psychotic symptoms. Antipsychotics, as previously described have been around for over 50 years, and although not a cure, they can assist in the prevention of the progression of the disease. They have however, been improved upon in what are now called "atypical antipsychotics." This advance in the pharmacology of antipsychotic drugs has been important in a number of ways. For example, they are better at addressing negative symptoms of the

disorder, they are less likely to cause extrapyramidal symptoms (Marder & Meibach, 1994; Tollefson, Beasley, Tamura, Tran, & Potvin, 1997; Small, Hirsch, Arvanitis, Miller, & Link, 1997) and tardive dyskinesia (Jeste, Lacro, Bailey, Rockwell, Harris, & Caleguir, 1999; Jeste, Rockwell, Harris, Lohr, & Lacro, 1999), and they have the potential for better outcomes in cognitive functioning than conventional antipsychotics (Kelleher, et al., 2002). Surprisingly however, studies have suggested that atypical antipsychotics have not greatly improved adherence rates; for example, Dolder and colleagues reported adherence rates of 54.9% for atypical antipsychotics versus 50.1% for conventional antipsychotics (Dolder, Lacro, Dunn & Jeste, 2002).

Adherence problems

Rates of poor medication adherence from 11% to 80% have been reported in various reviews of patients with psychotic disorders in various settings. While there are a number of reasons for such a large disparity (from patient characteristics to adverse side-effects), Van Putten attributed it to the subjective effect of the drugs, noting that 62% of schizophrenic inpatients who were dysphoric on their medications eventually refused further medication, while this only occurred with 11% of the patients who were syntonic (Van Putten, 1984). Average nonadherence increases from about 50% at 1 year after discharge from a psychiatric hospitalization, to 75% by the end of the second year after discharge (Corrigan, 1990; Fenton, Blyler, & Heissen, 1997; Weiden et al., 1991).

More recent reviews have been more specific in their reports of non-adherence, looking specifically at non-adherence to both attending appointments and taking prescribed medications (Nose, Barbui & Tansella, 2003). Using data from 103 studies, Nose et al. suggest that approximately 24% of individuals studied are non-adherent to keeping scheduled appointments while approximately 30% are non-adherent to medications. Given the growing emphasis on early intervention and the increasing evidence that early treatment with antipsychotic drugs may improve overall outcome in schizophrenia (McGlashan, 1998), ensuring medication adherence is particularly important when treating patients with a schizophrenic illness.

Several factors account for non-adherence to medication (Fenton, Blyler, & Heinssen, 1997); these factors may be classified as patient related (illness severity, lack of insight, and concomitant substance abuse), medication related (extrapyramidal and other side effects, unwieldy medication regime), treatment provider related (inadequate therapeutic alliance) and support system related factors (poor family support or supervision, financial or other barriers). Poor medication adherence early during treatment, inadequate discharge planning and immediate post-discharge care also predict poor adherence over the subsequent course of the illness (Lacro, Dunn, Dolder, Leckband, & Jeste, 2002). Impaired executive cognitive functions also predict a higher likelihood of medication discontinuation in first episode psychoses (Robinson et al., 2002). Finally, Nose and colleagues (2003) specifically identified many of the previously mentioned factors (lack of insight, substance abuse) as well as adding factors such as

positive symptoms, younger age, male gender, unemployment and low social functioning.

Interventions to increase adherence

Several intervention techniques have been developed to address medication non-adherence. Three of these have received the most attention in the literature: psychoeducation, behavioral training, and compliance therapy.

Psychoeducational methods involve helping individuals to understand more about their illness and medications, (e.g., the positive effects of taking medications, and the negative consequences of not taking medications) so that they might be better able to participate in the decision making process involved in their treatment (Gray, Wykes & Gournay, 2002) and has been one of the most widely researched areas for intervention. Individual medication regimens are carefully reviewed in order to insure that they are completely understood by the patient and this can be done in either a group or individual format.

Streicker and colleagues (Streicker, Amdur & Dincin, 1986) designed a study that consisted of two parts. First, they conducted a six-session didactic presentation that explained the biochemical theory of schizophrenia, reviewed the major psychiatric medications, and stressed the risks involved with illicit substance use. The second part consisted of a 4-week period of weekly discussions aimed at the importance of compliance, its long-term benefits, and communication with the treating physician. Patients were assessed at baseline and immediately post-intervention, as well as at a 35-week follow-up. While overall self-satisfaction and medication knowledge increased, there was no

significant between-group difference in adherence. Another study looking at group psychoeducation occurring every 2 weeks over an 8-week period also found no increase in adherence (Smith, Birchwood & Haddrell, 1992).

Numerous studies have also looked at the effect of individual psychoeducation. One such study randomly assigned patients to one of 4 groups: verbal information about medication, verbal and written information about medication, verbal information about medication and their side-effects, and verbal and written information about medications and their side-effects (Brown, Wright & Christensen, 1987). Similar to the previously reviewed studies, there was an increase in patient knowledge, but no significant effect on adherence. Other studies have had similar results (MacPherson, Jerrom, & Hughes 1996; Gray, Wykes, & Gournay 2000). Overall, studies that have evaluated psychoeducational approaches to improve adherence to treatment suggest that such approaches increase knowledge about treatment but do not affect either attitude or adherence behavior.

Behavioral tailoring/training interventions (e.g., Boczkowski, Zeichner, & DeSanto, 1985; Cramer & Rosenheck, 1999) focus on helping patients develop specific cues that incorporate aspects of their daily routine or environment to facilitate medication adherence. For example, patients may be encouraged to pair medication intake with a particular part of the daily routine, to identify a highly visible location for medication bottles, or to design a calendar with reminders that are to be removed after the administration of each dose. Boczkowski (1985) randomly assigned patients into behavioral tailoring,

psychoeducation, and control conditions. As measured by pill count alone, adherence was significantly improved in the behavioral tailoring condition, but not in the other two conditions. However, patient and observer ratings of adherence did not improve. Whether this reflects high initial adherence ratings, inaccurate self-report, or adjusting the number of pills turned in for counting (in order to appear more adherent) is unclear.

Cognitive-behavioral interventions have also been applied to the problem of medication adherence. Lecompte and Pelc (1996) examined five different approaches to facilitating medication adherence: psychoeducation, correcting false beliefs about medications, engaging the patient, identifying prodromal symptoms/developing coping strategies and behavioral interventions aimed at reinforcing adherent behavior. The patients receiving the Cognitive-behavioral interventions spent significantly less time in the hospital than the control group. Whether this was due to improved coping skills or increased medication adherence is unclear.

In a precursor study of what would eventually become compliance therapy, Hayward & Chan (1995) piloted an intervention based on the principles of motivational interviewing, designed to improve medication adherence. Although the effects did not reach statistical significance, the individuals receiving the intervention showed improvements in their attitudes towards medications and their insight into their illness. The authors believed that the small sample size of their treatment group contributed to the lack of significant findings, and were

impressed enough with their results to further adapt this intervention for future use. The result of this adaptation is discussed below.

Compliance Therapy (Kemp at al., 1996) is based in part on the principles of Motivational Interviewing (Miller & Rollnick, 1991). Compliance Therapy involves a 4- to 6-session intervention using motivational techniques along with psychoeducation and cognitive behavioral techniques (complete details are available in the published manual, Kemp, Hayward & David, 1997). The goal is to provide information about the benefits and side effects of medications; to highlight discrepancies between patients' actions and beliefs, provide positive reinforcement for adaptive behaviors; to emphasize the value of staying well; and to encourage self-efficacy with respect to taking medications. The evidence for compliance therapy is mixed, with Kemp and colleagues showing a positive effect on adherence (Kemp et al, 1996; Kemp, Kirov, Everitt, Hayward, & David, 1998) while replications by other research groups show no significant effects (Gray, et al, 2006, Byerly et al., 2005, O'Donnell et. al., 2003).

Interestingly, a recent comprehensive review of compliance therapy for the treatment of schizophrenia (McIntosh, Conlon, Lawrie, & Stanfield, 2007) did not include work by Kemp and colleagues because participants in these studies included individuals with "primary affective disorder". Even after widening the inclusion criteria to include studies wherein as few as 80% of participating individuals had to be diagnosed with schizophrenia or *related psychotic illness,* the work by Kemp and colleagues did not meet criteria. The review was able to identify only one study that met this criterion and was based solely on the

components of compliance therapy, i.e., it excluded studies that added another intervention, or did not target medication adherence. In that single study (O'Donnell, 2003), there was no significant effect of compliance therapy on medication adherence.

Despite some positive findings, then, Compliance Therapy appears to be of questionable applicability to treatment adherence among persons with schizophrenia. First, studies finding positive effects have included significant proportions of persons whose primary diagnosis was not schizophrenia. Second, the positive findings from the intervention's originators have not yet been successfully replicated by other research groups.

Overall, efforts to facilitate medication and other treatment adherence among persons with schizophrenia have not yielded a clearly supported approach. Psychoeducational approaches lead to increased knowledge about anti-psychotic medications but not to increased medication adherence. Behavioral training approaches seem to have some impact on adherence but have ultimately been inconclusive. They are also very costly and time consuming, and dissemination may be difficult to achieve. Research on cognitive approaches is limited and has not directly impacted adherence, although there is some evidence that it may have a positive impact on reducing hospitalizations. Compliance Therapy has produced some promising results but has not been reliably replicated. There is therefore a clear need to examine other possible approaches to treatment adherence in schizophrenia. It is also important to look seriously at the difficulty of disseminating potentially efficacious treatments.

Motivational interviewing: A Potential New Direction

Motivational interviewing (MI) is a brief, client-centered, yet directive method of facilitating health behavior change among persons who are not initially ready to change. It has been proven effective in addressing treatment adherence as well as behavioral change (Rubak, et al., 2005; Burke et al., 2003). Furthermore, MI has already shown efficacy with individuals suffering from schizophrenia. Steinberg et al. (2004) found that participants with schizophrenia receiving just one session of MI were significantly more likely to (a) contact a treatment provider regarding their tobacco use, and (b) attend their first scheduled session, when compared to participants given standard psychoeducational counseling or advice only. In a study designed to address comorbidity of substance abuse and schizophrenia, Barrowclough and colleagues combined MI, cognitive behavioral therapy, and a family intervention conducted over a 9-month period and found a significant improvement in overall functioning (Barrowclough, et al., 2001). The MI aspect of the intervention was the initial phase of treatment, designed to engage individuals who may be ambivalent about their drug use or treatment regimen. In other studies as well, MI has been proven particularly effective in encouraging individuals to take advantage of treatment options open to them, rather than necessarily being the primary treatment itself (Burke et al., 2003).

Although an effective method of bringing about behavior change, MI was empirically derived and there has been a dearth of research into the underlying theory that may explain the reasons for its success. Self-determination theory

(SDT; Deci & Ryan, 1985, 2000, 2002) has been recently posited as an explanatory theory that integrates well with motivational interviewing, providing finer and more explicit definitions of the motivational constructs that MI specifically targets (Markland, Ryan, Tobin & Rollnick, 2005; Vansteenkiste & Sheldon, 2006). Specifically, SDT suggests that behavior change takes place when an individual's needs are met in an as autonomous manner as possible. Theorists have thus suggested that MI may in part work through highlighting this autonomy by supporting the individuals' self-efficacy while helping them to reconcile the discrepancies that have kept them from doing so previously.

MI may thus be worth testing for its ability to facilitate medication and therapy adherence among persons with schizophrenia. However, as noted above, compliance therapy is in part based on the principles of MI and has not performed well in replication studies. A possible explanation for this finding lies in studies of moderators of the efficacy of MI, which together suggest that although MI is quite efficacious with persons who are not motivated to change, it may be ineffective or even counter-productive with persons who are already motivated to change. For example, Rohsenow and colleagues found that patients with higher levels of motivation prior to treatment reported less cocaine use and less severe alcohol problems during the following year if they did not receive motivational treatment (Rohsenow, Monti, Martin, et al., 2004). Similarly, Stotts et al. reported that MI treatment appeared to have a detrimental effect on individuals with high initial motivation (Stotts, Schmitz, Rhoades, & Grabowski 2001). Such findings suggest that, despite the weak evidence in favor of

compliance therapy (which includes a motivational component), motivational interviewing approaches may yet be helpful with this population if baseline motivation to change is taken into account.

Computer-Based Approaches: A Potential Solution for Dissemination Problems

Computer-based interventions have the potential to reach a large number of individuals at a substantially lower cost, both in terms of monetary expenditure as well as hours of time, training, and supervision usually required by many therapeutic interventions. These advantages give computer-based approaches great potential in terms of *population impact,* which can be described roughly as the product of an intervention's effect size, the percent of eligible persons in the community who experience that intervention, and the percent decrement in effect size when that intervention is replicated in the community (Smeeth & Ebrahim, 2000).

Given the ability of computer-based approaches to potentially impact a substantially larger number of individuals than would otherwise be possible, many researchers are beginning to examine this paradigm in a number of different areas. For example, computerized cognitive behavioral therapy has been found to result in clinically significant improvements in self-reports of anxiety and depression (Cavanagh, et al., 2006). In a study of MI-based computer-only feedback, greater reductions in drinking behavior among heavy-drinking college students were evident among computer-based feedback intervention participants relative to controls (Neighbors, Larimer and Lewis, 2004). Kiene and Barta (2006) used motivational interviewing techniques in a

study that looked at computer-delivered HIV/AIDS risk-reduction information. Participants displayed greater condom-related knowledge at a 4-week follow-up, as well as a significant increase in self-reported condom use. A computer-based motivational interviewing intervention designed to reduce perinatal drug use led to decreases in drug use as measured at a 4-month follow-up (Ondersma, Svikis, & Schuster, 2007). Finally, computer-based paradigms have been used for more than just therapeutic intervention. In a study of geriatric individuals, interactive computer programs were found to be effective in therapy, recreation and educational domains (McConatha, McConatha, Deaner and Dermigny, 1995).

Importantly, computer-based interventions have proven remarkably easy to use, even for persons with low reading or computer literacy (Ondersma, Chase, Svikis & Schuster, 2005). The clear, self-paced, visual and aural presentation of these interventions may be ideal for persons with schizophrenia, who may appreciate having the ability to set their own pace, as well as to experience different media while doing so. Certainly, some persons with schizophrenia may have difficulty with a computer presentation. However, the potential is clear; the actual proportion of persons with schizophrenia who can use computer-based approaches is an important empirical question.

Summary

Schizophrenia is a devastating illness with far ranging effects on both the individual and society. Relatively effective treatments for schizophrenia are available, but many patients do not adhere to their treatment regimens, resulting in relapses and increased severity and duration of illness. Also, dissemination of

these treatments can pose problems for many service providers. Interventions designed to address this adherence problem have shown mixed results, perhaps in part because they have (a) focused too strongly on educational approaches; (b) collapsed across baseline motivation to change, and (c) been difficult to disseminate. This study will therefore examine a tailored, computer-based motivational approach to adherence in schizophrenia. This approach will focus much more strongly on motivation than on education and knowledge, will be tailored to each individual patient's motivation to adhere to their medication regimen, and—if successful—will be far more replicable than previous adherence interventions.

Objectives and Hypotheses:

The main objective of the proposed study is to evaluate the feasibility, acceptability and potential efficacy of a computer-based motivational intervention designed to facilitate adherence to antipsychotic medication with individuals diagnosed with schizophrenia.

Primary Hypotheses:

It is expected that the computer-delivered motivational intervention will demonstrate good feasibility and acceptability with this population. It is also predicted that, H_1: patients randomly assigned to a computer-based motivational adherence intervention show higher rates of adherence to antipsychotic medication at follow-up, compared to patients assigned to a treatment-as-usual control condition.

Secondary Hypotheses:

H_2: Patients receiving computer-delivered motivational interviewing will show greater improvement at time 2 compared to patients in the control condition on the following variables: quality of life (community functioning, social relations, occupational functioning, and daily activities) and global functioning. H_{2a}: these differences will be mediated by medication adherence.

Chapter 2

METHOD

Participants

Participants were individuals attending the University Psychiatric Center's Services for the Treatment of Early-onset Psychosis (STEP) program and the schizophrenia clinic at the Arab-American Chaldean Council in Detroit, MI. Participants were all currently in treatment and were referred to the study by their psychiatrist, therapist, or social worker. A total of 51 participants were recruited to participate in this study. Participants ranged in age from 18 to 52. Persons of minority race and ethnicity make up approximately 85% of patients in these clinics; most are low-income and the recipients of public assistance, although a substantial minority (approximately 25%) have private medical insurance. All participants provided written informed consent. The Wayne State University Institutional Review Board approved all procedures used in this study.

Inclusion/exclusion criteria

All individuals enrolled in the clinics who are currently on medication for psychotic symptoms were eligible. Exclusion criteria included a current significant medical illness temporally related to psychosis. Due to the nature of psychotic illnesses, the diagnostic process can be elaborate, comprehensive and ongoing. The clinical team (Director of clinical programs, intake coordinators, trained research coordinators, clinical psychologists and psychiatrists) makes the initial diagnosis with all available information and this diagnosis rarely changes without additional information. Length of stay in this program is dictated by the

patient's stability (direct observations by clinical staff, self-report, as well as reports from involved significant others).

Procedure

Patients were told of the study, and their freedom to decline participation, by medical staff from the clinic. Participants were approached while in the waiting area, and if interested were directed to the researcher. The study was then briefly described for all interested clinic patients; those who remained interested were screened for eligibility. Eligibility requirements included a short, 5-question post consent form (Appendix 1) designed to ensure understanding of the consent process and the participant's rights, as well as the Mini-Mental Status Exam. Those eligible received full informed consent dialogue; those who agreed to participate and signed informed consent were included in the study. Participants were recruited by one of the members of the clinical team and were either taken immediately to a separate room for the computer session or scheduled for a later time. Immediately following the initial session, participants were scheduled for their follow-up session (4-6 weeks later). During the initial session, the computer randomly assigned participants into two groups. Both groups completed all study-related measures, but one group received the computer-based intervention, while the other received only an innocuous attention-control session involving television show clips and music videos. Participants received a $10.00 gift card for each treatment/data collection session. A clinic-based follow-up session ranged from 26 to 147 days, with a

mean interval of 44.35 days following the initial intervention/attention control session.

Assessment

Data regarding diagnosis (made by clinic staff using the SCID-IV) was gathered from clinic staff. All other data were collected via audio computer assisted self-interview technology (A-CASI; see “software” section, below). All data were collected at both of the observations, and took approximately 30-45 minutes initially and 15-20 minutes at follow-up; evaluations were kept brief to maximize the ability of participants to complete assessment without fatigue. Measures used included:

1. *Medication Adherence Rating Scale (MARS).* The MARS was created as a tool to replace the Drug Attitude Inventory (DAI, Hogan, Awad, & Eastwood, 1983) as the predominant measure of medication adherence for psychoses (Thompson, Kulkarni, & Sergejew, 2000). It is an easily administered, 10-item self-report questionnaire. Its main asset is the ease with which it can be administered and interpreted. In reliability/validity testing it was compared to the DAI and the Medication Adherence Questionnaire (MAQ, Morisky, Green, & Levine, 1986). The reliability analysis of the MARS using Cronbach’s alpha was 0.75, compared to 0.76 for the MAQ and 0.77 for the DAI. The test-retest reliability assessed after a 2-week interval using parallel-forms Chi-square was 0.72 for the MARS, 0.76 for the MAQ and 0.60 for the DAI. A multi-trait-multimethod matrix was used to measure construct validity. It correlated the total compliance score for each questionnaire with a caretaker’s estimation of compliance and blood levels

of medication. The MARS significantly correlated with other measures of compliance, showed no relationship with the caretaker's estimate, and was more strongly associated with blood levels of medication than the MAQ.

2. *Readiness rulers*. Readiness rulers are a visual analogue scale rating of motivation and confidence regarding medication.
3. *Social Adjustment Scale* (SAS; Weissman & Bothwell, 1976). The SAS is a 54-item measure of adaptive functioning within a variety of social contexts. The SAS has a global index and subscales providing information about a number of role areas: work, social and leisure activities, relationships with extended family, marital role, parental role, family unit role, and economic role. The SAS has fair internal consistency, with an alpha of .74, and good stability, with a one-month test-retest correlation of .74. The SAS also has fair concurrent validity, correlating with the social adjustment structured interview upon which it is based, and good know-group validity, distinguishing a non-clinical, community sample from three psychiatric samples and distinguishing acutely depressed from recovered clients.

Computer-based motivational intervention

The following description is taken directly from the software developers in order to illustrate that the identical software was utilized as was previously reported by Ondersma and colleagues. The software consists of an assessment section and an intervention section. The assessment section presents questions one at a time using a visually attractive screen that provides only the most pertinent information for the participant. Pleasant and relevant graphics

accompany each screen change to engage participants and help to maintain interest. A three-dimensional cartoon character (in the form of a parrot) capable of over 50 specific animated actions (e.g., smile, wave, read a message, express concern, etc.) does the “talking” for the entire program (Ondersma, Chase, Svikis & Schuster, 2005). This character “interacts” with each participant by guiding them through the presentation in a light-hearted manner, providing occasional humor while narrating assessment items in a relaxed, engaging setting. Participants listen to the narrator via headphones to insure privacy.

The intervention was based on motivational interviewing and brief intervention principles, and included three components:

1. Feedback regarding concerns about the diagnosis and medication regimen, as well as of the participant’s self-reported motivation (importance and confidence) to adhere to their medication.
2. Pros and cons of medication adherence, as well as pros and cons of continuing without medication.
3. A short video testimonial given by a Caucasian woman regarding her experience with her first psychotic episode and how medication was able to assist her in her recovery, and (in keeping with the tenets of motivational interviewing) the importance of her participation – and to some degree control – in her own medical care.
4. A summary and query regarding the participant’s interest in beginning a structured adherence program; those who indicated readiness to do so

completed a change plan that assisted them in specifying exactly what their medication goals were.

Throughout the intervention, the animated narrator helped clarify the participant's answers by "reflecting" the participant's answers back to them, in a non-judgmental, reworded manner that served to assure the participant that he or she is being understood, reflecting an atmosphere consistent with that provided by an actual motivational interviewing practitioner. Participant's second interaction with the computer at follow-up repeated the initial assessments as well as administered a 10 question assessment on their opinions about the intervention itself. All individuals who completed the initial assessments were compensated for their time as stated above.

Control condition

Individuals in the control condition interacted with the computer by watching innocuous videos and answering questions about those videos. This condition was designed to be indistinguishable from the intervention condition to anyone not watching the computer screen.

Regardless of the condition, in all situations, a linking table was used to connect names to the data. This linking table was kept in a locked file cabinet, to which only two persons had access.

Chapter 3

RESULTS

DATA ANALYSIS

A. Missing data analysis

Patterns of missing data were examined. No missing data were found for either of the primary assessment measures.

B. Data screening procedures

Data were analyzed using SPSS version 18 (SPSS, Chicago: SPSS Inc). All data were initially examined for skew, kurtosis, and out of range values, homoscedasticity (homogeneity of variance), and univariate outliers. Histogram analysis revealed possible skewness, and was confirmed by a skewness factor larger than two times the standard error of skew. For the MARS, both baseline and follow-up data were moderately positively skewed and were therefore normalized using the logarithmic transformation. The baseline SAS data were substantially skewed, and therefore both baseline and follow-up SAS data were normalized using the logarithmic transformation. The transformations were successful. Homoscedasticity was assessed using Levene's Test within independent samples t-tests; results were not significant (all *p*'s > .10).

C. Participant flow

Participant flow is summarized in Figure 1. A total of 78 participants were approached regarding the study; 53 (67.9%) were interested and agreed to be screened. Two men (3.8%) were unable to pass the post consent quiz that was designed to ensure participant's understanding of the informed consent process

and were therefore excluded. Therefore, 51 (96.2%) met the inclusion criteria for participation and were randomized. Additionally, two men who consented were interrupted during their baseline assessment and did not complete this portion of the study, leaving a total of 49 eligible for follow-up, with 24 receiving the intervention, and 25 receiving assessment only (control). A total of 43 (87.8%) completed follow-up assessment (follow-up ranged from 26 to 147 days, mean of 44.35 days), with three men lost from each group at follow-up.

C. Participant characteristics

All patients were diagnosed with schizophrenia and had been prescribed medication. Participants were on average high school educated and predominantly African American. Consistent with the epidemiological characteristics of schizophrenia, there were more males than females. Sample characteristics are reported in Table 2.

D. Evaluation of group equivalence at baseline and follow-up

To assess randomization success at baseline, comparisons of demographic characteristics between intervention and control groups were conducted with *t* tests for normally distributed continuous characteristics (age and education) and chi-square tests for categorical data (gender, race). Independent samples t-test analyses revealed no significant differences in demographic characteristics between the intervention and control groups at baseline. Similarly, chi-square analysis revealed no significant differences in gender or race (Table 3).

Retention was good overall, with 43 out of 49 participants (87.8%) assessed at follow-up. Of these, 21 of 24 (87.5%) were from the intervention condition and 22 of 25 (88%) were from the control condition. Data from drop-outs were examined by comparing those who completed the follow-up (n = 43) to those who dropped out (n = 6) by treatment status and by baseline characteristics. No significant differences were found (all *p*'s > .39); these missing data were therefore not seen as threatening the validity of the study.

E. Evaluation of study measures

The range, mean, and standard deviation for all study measures are reported in Table 4. The current sample scored lower on quality of life (SAS) than would be expected from normative data for a similar population, specifically in the areas of "primary relationship" and "family unit". Bivariate correlations between all study measures, including SAS subscales, are reported in Table 5.

F. *Intervention feasibility and acceptability*

With respect to feasibility, all participants reported that they experienced no problems with the program, and were able to complete the study. One participant stated that he preferred not to participate after being introduced to the program and dropped out of the study.

Results from the assessment of software assessment/intervention acceptability are displayed in Table 1. Scores for acceptability could range from 1 – 5 on a Likert-type scale. All items except for questions 4 and 9 were reverse-coded such that higher scores indicated greater acceptability. Table 1 shows means and standard deviations for each acceptability item, demonstrating that

mean acceptability was over 4 for all positively-worded items. The two negatively-worded items designed to pull for negative responses (“How much did some parts of the computer bother you?” and “How uncomfortable were you working with Peedy the bird?”) had mean ratings of 3.7 and 3.9, respectively.

G. Preliminary Efficacy

Primary Hypothesis 1: Medication adherence.

The main objective of the study was to evaluate the acceptability and initial efficacy of a computer-based motivational intervention designed to facilitate adherence to antipsychotic medication. The first of two primary hypotheses was that patients randomly assigned to the computer-based motivational adherence intervention would show higher rates of adherence to antipsychotic medication at follow-up, compared to patients assigned to the control condition. This was tested via a General Linear Model using the MARS as the repeated measures factor (measured at baseline and follow-up). Patients randomly assigned to the computer-based motivational adherence intervention did not show higher rates of adherence to antipsychotic medication at follow-up, as measured by the MARS, compared to patients assigned to the control condition, $F(1, 41) = .12$, $p = .73$ (Table 6).

Primary Hypothesis 2: Quality of life

The second primary hypothesis was that patients in the experimental condition would show greater improvement compared to patients in the control condition on a global measure of quality of life (lower scores on the SAS scale). This was tested via a General Linear Model where quality of life was a repeated

measures factor (baseline and follow-up). Compared to patients assigned to the control condition, patients randomly assigned to the computer-based motivational adherence intervention did not show improved quality of life on the SAS scale at follow-up, $F(1, 41) = .43$, $p = .52$ (Table 6).

Secondary Analyses

Secondary analyses first focused on exploratory evaluation of potential moderators, to examine whether intervention effects may have been present in some subgroups of participants. Four specific variables were examined as potential moderators: baseline MARS score and baseline SAS score (to examine whether treatment effects varied with level of initial adherence or quality of life), gender, and follow-up delay (time between baseline and follow-up). Continuous variables were dichotomized using a median split and were entered into 2 X 2 Factorial ANOVAs along with intervention condition (intervention vs. control). The interaction term was then examined for evidence that the effect of the intervention differed based on the baseline value of each of the four variables being examined. When the moderator was gender and follow-up delay, the dependent variable used was the change score of SAS and MARS which was derived by subtracting the baseline value from the follow-up score. The dependent variable was the time two value when the moderator being considered was itself at time one, (i.e., baseline MARS scores as a moderator of MARS outcomes and baseline SAS scores as moderator of SAS outcomes). As seen in Table 7, these analyses did not provide any evidence of moderation of intervention effects.

Secondary analyses next focused on examination of change in medication adherence and quality of life overall (i.e., regardless of intervention condition), and predictors of that change. As seen in Figure 2, the sample as a whole declined on medication adherence attitudes as measured by the MARS, and increased slightly on quality of life as measured by the SAS (scores slightly decreased). Two separate linear regressions were run, exploring the association between demographic variables and adherence/quality of life as measured at baseline (education level, race, gender and age; entered simultaneously) with change score derived from each of the two primary outcomes. The overall model for the SAS change score ($F(4, 34) = .98$, $p = .43$) was not significant, nor were any of the four individual measures. The overall model for the MARS change score ($F(4,34) = .64$, $p = .64$) was not significant, nor were any of the 4 individual measures.

As noted above, importance and confidence were only measured at baseline for participants assigned to the intervention condition. In a separate multiple regression, the treatment-only variables of baseline importance and confidence were added to the overall model for the MARS and SAS change scores. The overall model for the SAS change score was not significant ($F(6,11) = 1.04$, $p = .45$), nor were any individual measures. The overall model for the MARS change score was also not significant ($F(6,11) = 2.69$, $p = .074$), but baseline importance was a significant predictor of change in medication adherence (standardized beta of -1.01, $t = -2.79$, $p < .018$). Specifically,

participants with higher importance scores at baseline were more likely to report attitudes reflecting worse medication adherence at follow-up.

Finally, given the wide range in follow-up delay, we examined whether there was any association between follow-up duration and outcomes. Spearman's Rho between follow-up duration and outcomes was not significant (r = .19 for follow-up MARS, p = .21, and r = -.21 for follow-up SAS, p = .18).

Chapter 4

DISCUSSION

The main objective of this study was to evaluate the feasibility, acceptability, and initial efficacy of a computer-based motivational intervention designed to facilitate adherence to antipsychotic medication among persons diagnosed with schizophrenia. Such an intervention, if acceptable, feasible, and efficacious, could do much to mitigate the substantial negative consequences of non-adherence among persons with schizophrenia.

Feasibility and acceptability must be determined first in the intervention development process, before fully engaging in the expensive and time-consuming process of evaluating efficacy. The 43 participants for whom follow-up data were obtained in this study provided strong evidence for feasibility and acceptability of computer-delivered approaches with this population. For example, most participants (87.8%) returned for a second session. Ratings of enjoyment, interest, utility and respectfulness were high, ranging from a low of 4.0 on a 1-5 scale (with 5 being best) for enjoyment of the bird's voice, and a high of 4.7 for perceived respectfulness of the bird towards the participant. Further, only one of the 51 participants in this study - despite all having a diagnosis of schizophrenia - was unable or unwilling to complete the brief session with the computer. These findings are extremely important, and bode well for the future of computer-delivered content with this population. There is evidence that computerized administration of cognitive remediation for individuals suffering from schizophrenia has been successful as well, adding further support

for utilizing computer-based strategies for this population (Cavallaro, Anselmetti, Poletti, Bechi, Ermoli, Cocchi et al., 2009; Kurtz, Seltzer, Shagan, Thime, & Wexler, 2007).

Demonstration that a specific form of such content can be efficacious is thus a key next step. In this very preliminary examination of the efficacy of one possible approach, there was no observed effect of the intervention on either attitudes surrounding adherence to medication or on measures of quality of life. The study sample overall showed only very small changes on either outcome over the follow-up period (mean of 44 days), with no evidence of an effect for treatment condition.

Despite the very small N, it was deemed appropriate to conduct preliminary examinations of whether intervention effects may have been present in some subgroups of participants, as such information can be valuable in guiding possible modifications to intervention approach. There was no evidence of moderation of intervention effects by baseline values of the primary outcome measures, by gender, or by follow-up interval. Although power to detect such effects is less than that for detecting main intervention group effects, this finding does suggest that genuine intervention effects were not likely to have been masked by subgroup effects. Of course, other (unmeasured) constructs could have acted as moderators of the intervention in this study, but the small overall changes regardless of condition suggest that this is not likely.

Participant's reports of their belief about the importance of taking their medication were associated with follow-up scores on attitudes about adherence.

That is, participants with higher importance scores at baseline were more likely to report attitudes reflecting worse medication adherence at follow-up. This was interesting, as it seems at first glance contradictory; it initially appears that participants may have been duplicitous in their original self-assessment of importance. It is possible however, that self-rated level of importance reflected an earnest belief on the part of participants, but added little to their ability to actually follow through with their desire to consistently take medication. It is also possible that individuals who rate this with high levels of importance may also hold themselves to a higher subjective standard. Finally, and consistent with SDT, it may be that one of the mechanisms that is posited to be responsible for behavior change - specifically that of autonomy- was not sufficiently addressed in this study. Given the fact that there is little choice for these individuals with regard to effective treatments, it may be that further highlighting the choices that are available to them would be suitable target for improving efficacy.

There are a number of possible reasons for the lack of overall intervention effect. These possibilities will be outlined below, along with limitations of the current study, implications of the findings, and possible future directions for research in this area.

Lack of Treatment Effect

A number of factors may account for the lack of treatment effect in the current study. First, and perhaps most parsimoniously, it is possible that there is not a simple treatment that provides an efficacious way of addressing the difficulties facing this particular population. As reviewed above, a number of

approaches have sought to assist individuals suffering from schizophrenia with medication adherence - with mixed success. The challenges facing this population are considerable and finding an “easy fix” that will allow them to circumvent their daily difficulties has been elusive at best. It may be that intensive, daily behavioral interventions are the only method whereby significant positive changes can be effected as discussed above, though even that evidence is not conclusive and appears to impact only certain domains, such as pill count (Boczkowski, 1985). However, as the current intervention was tolerated and even liked by participants, computer-delivered motivational interventions may help to increase motivation to participate in daily behavioral interventions. This bodes well for the possibility of utilizing the current intervention to focus solely on motivation for engaging in other more intensive interventions such as behavioral based treatments. There is evidence that motivational interviewing is useful as a precursor to other established standard treatments (Hettema, Steele & Miller, 2005). The savings in cost and time garnered by utilizing the computer administered treatment may be an ideal way of providing this precursor. There are also other possibilities why the current intervention was unable to yield significant results.

First, as reviewed above, there has been some evidence from other research that motivational interviewing can have success with individuals suffering from schizophrenia, but it may be that this specific intervention is not the optimal way of providing it. It is also a possibility that the method of delivery via computer did not provide sufficient means for presenting the intervention.

Due to the nature of this illness, it is possible that internal stimuli make it difficult for participants to remain focused on the task at hand, and as a result may have a negative impact on their ability to adequately and accurately report their current feelings or state of mind. Also, it is possible that attending to the program's cartoon narrator is too distracting to allow them to switch their focus from him to their own internal state and back again.

In addition, there is evidence from other literatures that, within a brief intervention format, there can be a dose-response relationship (e.g., Burke et al., 2003). It may be the case that presenting a similar intervention on a more regular and repetitive basis would enable participants to derive more from the intervention than a single session can provide. For example, brief interventions for smoking become progressively more efficacious as the number of repetitions and/or total duration increases, but only up to an approximate 4 session/30-minute limit (Fiore, Jaen, Baker, Bailey, Benowitz, & Curry et al.,2008).

Focusing still on the pervasive nature of schizophrenia, it is important to note that this sample scored worse on the SAS at baseline than would be expected based on normative data from a similar population. Notably, the two subscales that the current population fared worst on were measures of what could be deemed as social support, namely, primary relationships and extended family. It can be argued that interventions to improve functioning among this group need to focus first on social support before targeting higher levels of self-actualization, in order to provide the foundation upon which other interventions might be built.

Another possible challenge to addressing the issue of medication adherence is that of adequate measurement. Relying solely on measures of adherence attitudes, although an accepted method of measurement in the literature (Thompson, Kulkarni, & Segejew, 2000), is not sufficient to capture actual medication adherence. Future studies, as was originally planned for this one, should include biomarkers of adherence such as presence of anti-psychotic medication in urine.

Additionally, as a pilot, early stage feasibility study, the N and consequent lack of power may have prevented detection of small but meaningful changes in adherence attitudes and quality of life. Even very small effects may have substantial importance given the consequences of non-adherence in this population, and the very inexpensive and replicable nature of computer-delivered approaches. As this sample consisted entirely of individuals actively participating in treatment, there may have been ceiling effects as they had less room to improve than individuals not in treatment, making an effect harder to detect.

Finally, this study utilized only a single follow-up point and a relatively short follow-up duration. Although motivational approaches in general can appear to have a relatively immediate effect that dissipates over time, there is strong evidence that there are often enduring or even delayed effects (Hettema, J., Steele, J., & Miller, W. 2005). Calendar-based recall (otherwise known as Timeline Followback approaches) could also add much to overall validity of adherence measurement. Sobell and colleagues found enduring effects of a brief motivational interviewing/cognitive behavioral approach on alcohol and drug

use and found enduring effects at 6 and 12 months post treatment (Sobell, Sobell & Agrawal, 2009).

Limitations

The limitations of the present study mirror many of the possible explanations of lack of treatment effect delineated above (e.g inadequate adherence measurement, small N); correcting for these may improve future research. In addition, there are other limitations that may have impacted the ability of this study to yield positive results. For example, the woman in the testimonial video represented only one ethnicity (Caucasian) and gender, while the majority of participants were African-American males. Further, the cartoon character, although well received, was the only option for individuals to choose from. It may also be that, if the resources to do so had been available, detailed focus groups with iterative modifications of the intervention may have yielded a better-targeted intervention. Finally, insufficient funds prohibited implementing more accurate measuring of actual medication intake, or at least biomarkers of medication levels, and this is key to obtaining a clear picture of medication use patterns over time.

Implications

The results of this study have at least two clear implications. First, it appears that many persons in treatment for psychotic disorders are able to utilize a computer-based format for assessment as well as for brief intervention. Issues regarding reality testing, anxiety, cognitive functioning, and others all may have suggested that this group would have difficulty with an animated narrator, but this

does not appear to have been the case. This finding opens up computer-delivered assessment and intervention as one new potential tool available for use among this population.

Second, these findings re-affirm that schizophrenia is a very complex disorder that impacts those who suffer from it in myriad ways, and does not lend itself to a simple, straightforward treatment that will have an immediate and enduring impact on all of those persons who undergo it. It seems clear that basic essential needs for some of these individuals need to be addressed first, as well as examining the problem of a lack of social support, which may have played a significant role in the current study's population.

Future Directions

This study accomplished the first goal of intervention development, demonstrating feasibility and acceptability. Future efficacy studies focusing on measures of motivation and biomarkers of adherence are necessary to determine the utility of the intervention. Given sufficient time and resources the current study could be improved by focusing specifically on piloting an intervention that brings into play many of the previously mentioned shortcomings. This ideal intervention would involve increasing the number of intervention points and allowing each to be tailored based on the responses given by the participant on their previous computer interaction. Shortening the duration between each treatment administration and having biomarkers for the detection of anti-psychotic medication in the system of the patient would provide a more accurate and reliable measure of adherence. It has also been suggested that electronic

monitoring in the form of MemsCAPS (pill bottles which record the times that patient's open them to take their medication) would also allow for feedback for participants, allowing them to follow their own progress and the researcher to adjust the intervention for them accordingly (Byerly, Fisher, Carmody, & Rush, J. (2005). Finally, giving the participants their choice of a number of possible characters with which to interact may further highlight their autonomy with regard to utilizing this particular intervention, as well as possibly enhancing their enjoyment of the same.

Appendix 1

Post-Consent Quiz

1. What is the study about?
2. Once you start, do you have to stay in the study if you don't want to?
3. Will you receive anything for your time and inconvenience?
4. Will anybody besides the researchers be able to see your answers?
5. If you have questions, is there a way for you to get in touch with someone from the study, to get some answers?

Appendix 2:

The Medication Adherence Rating Scale (MARS)

Please respond to the following statements by circling the answer which best describes your behaviour or the attitude you have held toward you medication in the past week.

1. Do you ever forget to take your medication? Yes/No
2. Are you careless at times about taking your medication? Yes/No
3. When you feel better, do you sometimes stop taking your medicine? Yes/No
4. Sometimes if you feel worse when you take the medicine, do you stop taking it? Yes/No
5. I take my medication only when I am sick. Yes/No
6. It is unnatural for my mind and body to be controlled by medication. Yes/No
7. My thoughts are clearer on medication. Yes/No
8. By staying on medication, I can prevent getting sick. Yes/No
9. I feel weird, like a ‘zombie’, on medication. Yes/No
10. Medication makes me feel tired and sluggish. Yes/No

Figure 1:

Consort Diagram

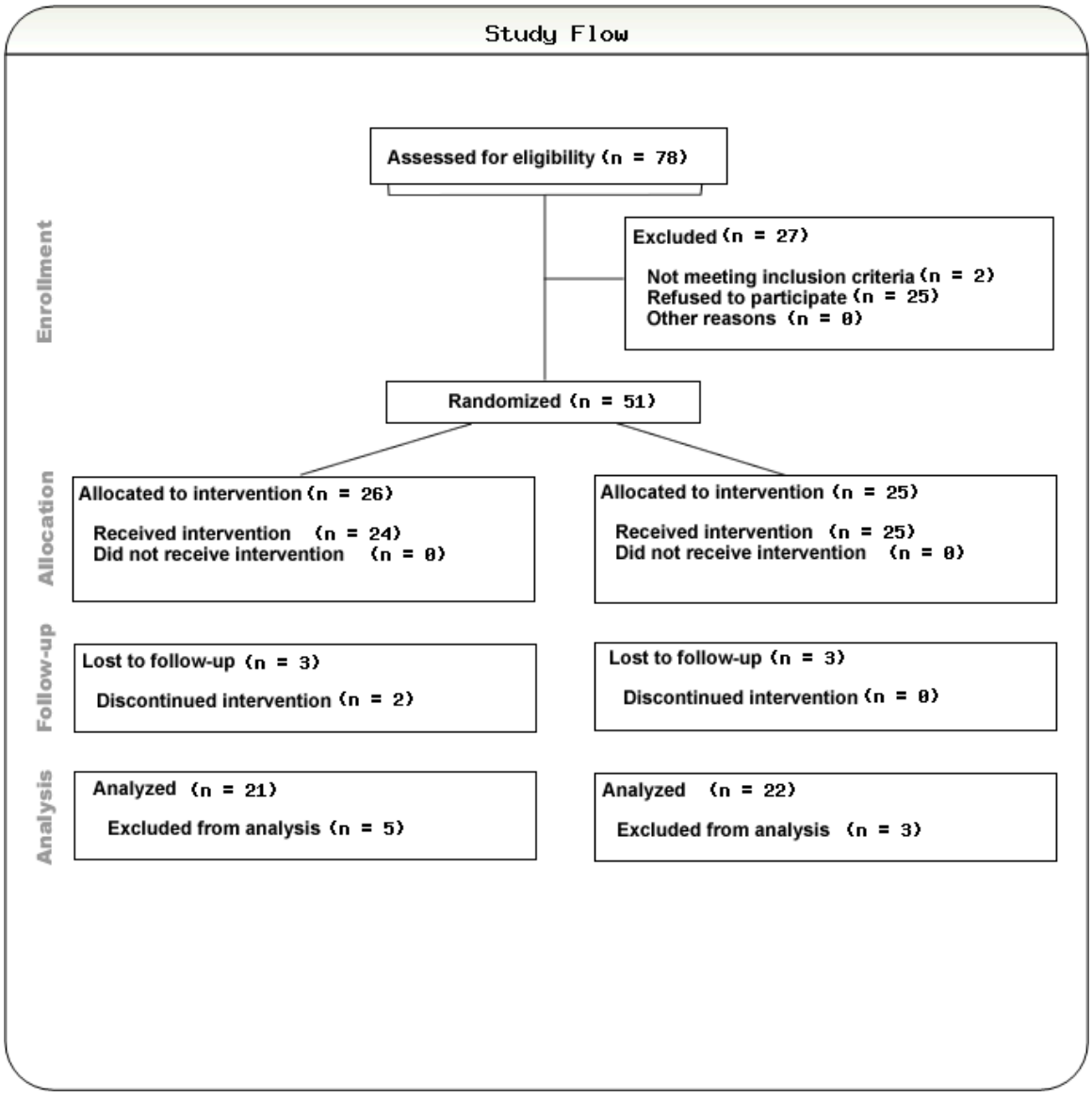


Table 1

Acceptability

Acceptability Questions:	N	Min.	Max.	Mean	SD
How much did you like working with the computer?	43	2	5	4.42	.96
How interesting was it?	43	2	5	4.19	1.03
Was it respectful of you?	43	2	5	4.67	.84
How much did some parts of the computer bother you?	43	1	5	3.70	1.28
How helpful was it for you?	43	1	5	4.21	1.15
How much did you like Peedy the bird?	43	1	5	4.47	1.08
How much did you like his voice?	43	1	5	4.00	1.29
How much did he help you think about your medication?	43	1	5	4.14	1.41
Were you uncomfortable working with Peedy the bird?	43	1	5	3.91	1.44
How clear and respectful was the researcher?	43	3	5	4.82	.53

Note. Possible responses ranged from 1 to 5; all items except #4 and #9 reverse coded so that higher scores universally suggest better acceptability.

Table 2
Sample Characteristics

Variable	Total (n = 49)	Range
Gender (%)		
Male	33 (67.3%)	
Female	16 (32.7%)	
Race (%)		
African American	31 (63.3%)	
Caucasian	7 (14.3%)	
Arab American	3 (6.1%)	
American Indian	1 (2.0%)	
Asian	1 (2.0%)	
More than one	4 (8.2%)	
Age (*SD*)	29.87 (10.47)	18-52
Years of education (*SD*)	12.80 (2.06)	8-18

Table 3

Baseline Characteristics, Intervention vs. Control

Variable	Intervention Mean ± *SD*	Control Mean ± *SD*	*t* or χ^2	*df*	*p*
Age (years)	29.10 ± 9.69	30.56 ± 11.27	-.48	45	.64
Education (years)	12.76 ± 1.93	12.83 ± 2.21	-.12	43	.91
Gender			.26	1	.61
Race*			4.33	2	.12

Note. Race was collapsed into African American, Caucasian, and other.

Table 4

Range, Mean, and Standard Deviations for all Study Measures (N = 49)

Measure	Range Actual (possible)	Mean/*n* (%)	*SD*
Taking Meds perfectly?		43 (87.8%)	
Importance Ruler (N = 24)	1-9 (1-10)	6.87	2.33
Confidence Ruler (N = 23)	4-9 (1-10)	7.57	1.75
MARS	0-9 (0-10)	3	2.38
SAS	32-107 (12-283)	2.09	.65
Work Role			
Work for Pay	1-23 (0-31)	1.49	.85
Housework	1-12 (0-31)	1.56	.92
Student	6-21 (0-33)	1.39	.67
Social and Leisure	15-50 (1-59)	2.42	.64
Extended Family	2-24 (1-40)	1.89	.84
Primary Relationship	14-31 (0-47)	2.67	.64
Parental	5-9 (0-21)	1.83	.52
Family Unit	1-16 (1-21)	2.29	1.30

Table 5

Zero-Order Correlations Between all Study Measures and Subscales

	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1 MARS	**.14**	**.76****	**.25**	**-.41***	**-.27**	**X**	**-.02**	**X**	**.26**	**.45****	**X**	**X**	**-.19**	**-.38****
2 SAS	**X**	**.22**	**.64****	**-.67****	**-.63****	**X**	**.63****	**X**	**.64****	**.72****	**X**	**X**	**.75****	**-.06**
3 MARS2		**X**	**.25**	**-.68****	**-.47***	**X**	**.06**	**X**	**.36***	**.47****	**X**	**X**	**-.15**	**-.22**
4 SAS2			**X**	**-.72****	**-.49***	**X**	**.04**	**X**	**.58****	**.54****	**X**	**X**	**.43****	**-.30**
5 Import				**X**	**.61****	**X**	**-.49**	**X**	**-.56****	**-.54****	**X**	**X**	**-.48***	**.32**
6 Confid					**X**	**X**	**-.38**	**X**	**-.63****	**-.44***	**X**	**X**	**-.41**	**.05**
7 Wk/pay						**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
8 Hswk							**X**	**X**	**.22**	**.32**	**X**	**X**	**.24**	**-.06**
9 Studen								**X**	**X**	**X**	**X**	**X**	**X**	**X**
10 Soclei									**X**	**.59****	**X**	**X**	**.24**	**-.09**
11 ExtFa										**X**	**X**	**X**	**.29***	**.00**
12 PrimR											**X**	**X**	**X**	**X**
13 Paren												**X**	**X**	**X**
14 Famu													**X**	**-.03**
15 Medsa														**X**

Definitions of abbreviations from above: MARS = Medication Adherence Rating Scale, SAS = Social Adjustment scale. MARS2/SAS2 = Same scales at follow-up. 5 = Importance. 6 = Confidence. The following are subscales of the SAS: 7 = Work for pay, 8 = Housework (unpaid), 9 = Student, 10 = Social and Leisure, 11 = Family outside the home, 12 = Primary Relationship, 13 = Parental, 14 = Family Unit, 15 = self report of medication adherence.

****. Correlation is significant at the .01 level.**

***. Correlation is significant at the .05 level.**

a. Cannot be computed because at least one variable is constant.

Correlations for subscales with an N of <14 were removed from the table.

Table 6

Summary of Intervention Effects (N = 43)

Outcome Variable	Estimated Marginal Means		*df*	*F*	*p*
	Baseline	Follow-up			
MARS*			1, 41	.12	.73
Intervention	3.71	3.33			
Control	2.09	1.64			
SAS			1, 41	.43	.52
Intervention	2.08	2.02			
Control	2.11	1.96			

* Significant difference at baseline between intervention and control, $p = .041$. Note: Baseline MARS and SAS values were controlled for in analyses of group differences at follow-up.

Table 7

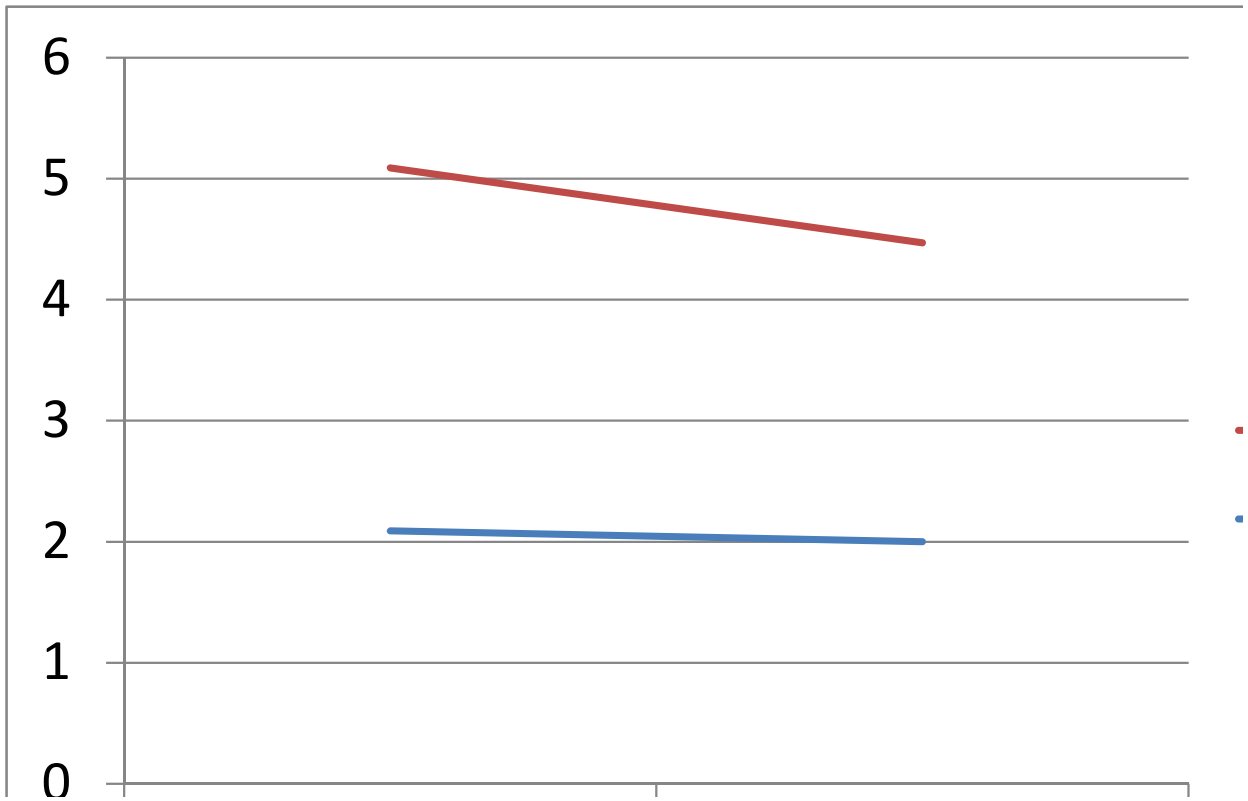
Moderator analyses

Outcome = MARS	*df*	*F*	*P*
Moderator: Baseline MARS			
Baseline MARS	1	19.16	.00
Intervention condition	1	2.66	.11
Baseline MARS x condition	1	1.17	.29
Moderator: Baseline SAS			
Baseline SAS	1	.05	.83
Intervention condition	1	.12	.73
Baseline SAS x condition	1	.02	.89
Moderator: Gender			
Gender	1	.08	.78
Intervention condition	1	.90	.35
Gender x condition	1	.03	.88
Moderator: Follow-up Delay			
Follow-up Delay	1	2.10	.16
Intervention condition	1	.21	.65
Follow-up Delay x condition	1	.81	.38

Outcome = SAS	*df*	*F*	*P*
Moderator: Baseline MARS			
Baseline MARS	1	.25	.62
Intervention condition	1	.59	.45
Baseline MARS x condition	1	.06	.80
Moderator: Baseline SAS			
Baseline SAS	1	22.94	.00
Intervention condition	1	.12	.74
Baseline SAS x condition	1	.81	.37
Moderator: Gender			
Gender	1	.61	.44
Intervention condition	1	2.83	.10
Gender x condition	1	.15	.70
Moderator: Follow-up Delay			
Follow-up Delay	1	5.93	.02
Intervention Condition	1	.16	.70
Follow-up Delay x condition	1	2.67	.11

Figure 2

Total Sample Change Over Time



REFERENCES

Andreasen, N. (1983). The specificity of Bleulerian and Schneiderian symptoms: A critical reevaluation. *Psychiatric Clinics of North America, 6*, 41-54.

Austin, J. (2005). Schizophrenia: an update and review. *Journal of Genetics and Counseling*, *14*, 329-340.

Ban, T. (2004). Neuropsychopharmacology and the genetics of schizophrenia: a history of the diagnosis of schizophrenia. *Progress in Neuropsychopharmacology and Biological Psychiatry*, *28*, 753-62.

Baron, R., & Kenny, D. (1986). The moderator-mediator variable distinction in social psychological research: Conceptual, strategic, and statistical considerations. *Journal of Personality and Social Psychology, 51*, 1173-1182.

Barrowclough, C., Haddock, G., Tarrier, N., Lewis, S., Moring, J., O'Brien, R., Schofield, N., &McGovern, J. (2001). Randomized controlled trial of motivational interviewing, cognitive behavior therapy, and family intervention for patients with comorbid schizophrenia and substance use disorders. *American Journal of Psychiatry*, *158*, 1706-1713.

Baumeister, A. & Francis, J. (2002). Historical development of the dopamine hypothesis of schizophrenia. *Journal of the History of the Neurosciences*, *11*, 265-277.

Bein, HJ. (1970). Biological research in the pharmaceutical industry with reserpine. In: Ayd, FJ., Blackwell, B. eds., *Discoveries in Biological Psychiatry*. Philidelphin, J.B. Lippincott Company, 142-154.

Bloom, FE (1993). Advancing a neurodevelopmental origin for schizophrenia. *Archives of General Psychiatry 50*, 224-227.

Boczkowski, J., Zeichner, A., & DeSanto, N. (1985). Neuroleptic compliance among chronic schizophrenic outpatients: an intervention outcome report. *Journal of Consulting and Clinical Psychology*, *53*, 666-671.

Brown, C., Wright, R., & Christensen, D. (1987). Association between type of medication instruction and patient knowledge, side-effects and compliance. *Hospital and Community Psychiatry*, *38*, 55-60.

Burke, B., Arkowitz, H., & Menchola, M. (2003). The efficacy of motivational interviewing: A meta-analysis of controlled clinical trials. *Journal of Consulting and Clinical Psychology, 71*, 843-861.

Byerly, M., Fisher, R., Carmody, T., & Rush, J. (2005). A trial of compliance therapy in outpatients with schizophrenia or schizoaffective disorder. *Journal of Clinical Psychiatry, 66*, 997-1001.

Carlsson, A., Lindqvist, M, & Magnusson. (1957). 3,4-Dihydroxyphenylalanine and 5-hydroxytryptophan as reserpine antagonists. *Nature*, *180*, 1200.

Carpenter, K. M., Watson, J. M., Raffety, B., & Chabal, C. (2003). Teaching Brief Interventions for Smoking Cessation Via an Interactive Computer-Based Tutorial. *Journal of Health Psychology*, *8*, 149-160.

Cavanagh, K., Shapiro, D., Van Den Berg, S., Swain, S., Barkham, M., & Proudfoot, J. (2006). The effectiveness of computerized cognitive behavioural therapy in routine care. *British Journal of Clinical Psychology, 45*, 499-514.

Corrigan, P.W., Lieberman, R.P., & Engel, J.D. (1990). From Non-compliance to collaboration in the Treatment of Schizophrenia. *Hospital and Community Psychiatry*, *41*, 1203-1211.

Cramer, J., & Rosenheck, R. (1999). Enhancing medication compliance for people with serious mental illness. *Journal of Nervous and Mental Disease*, *187*, 53-55.

Deci, E.L., & Ryan, R.M. (1985). *Intrinsic motivation and self-determination in human behavior*. New York: Plenum.

Deci, E.L., & Ryan, R.M. (2000). The what and the why of goal pursuits: Human needs and the self-determination of behavior. *Psychological inquiry, 11*, 227-268.

Deci, E.L., & Ryan, R.M. (2002). *Handbook of self-determination research*. Rochester: The University of Rochester Pres.

Deniker, P. (1983). [Psychopharmacology and biologic psychiatry. Historical review] Article in French. *Soins Psychiatrie*, *37*, 5-6.

Dolder, C., Lacro, J., Dunn L., & Jeste, D. (2002). Antipsychotic medication adherence: is there a difference between typical and atypical agents? *American Journal of Psychiatry*, *159*, 103-108.

Evans, K., McGrath, J., & Milns. (2003). Searching for schizophrenia in ancient Greek and Roman literature: a systematic review. *Acta Psychiatrica Scandinavica*, *107*, 323-330.

Feinberg, I. (1990). Cortical pruning and the development of schizophrenia. *Schizophrenic Bulletin*. *16*, 567-70.

Feinberg, I. (1982). Schizophrenia: Caused by a fault in programmed synaptic elimination during adolescence? *Journal of Psychiatric Research*, *17*, 319-334.

Fenton, W., Blyler, C., & Heinssen, R. (1997). Determinants of medication compliance in schizophrenia: empirical and clinical findings. *Schizophrenia Bulletin*, *23*, 637-651.

Fenton, W., & McGlashan, T. (1992). Testing systems for assessment of negative symptoms in schizophrenia. Archives of General Psychiatry, *49*, 236-237.

Fiore MC, Jaen CR, Baker TB, Bailey, W., Benowitz, N., Curry, S. et al. (2008). *Treating Tobacco Use and Dependence: 2008 Update.* Clinical Practice Guideline. Rockville, MD: U.S. Department of Health and Human Services. Public Health Service.

Gaddum, JH. (1954). Drugs antagonistic to 5-hydroxy-tryptamine. In: Wolstenholme GEW., Cameron, MP., eds., *CIBA Foundation Symposium on Hypertension, Humoral and Neurogenic Factors*. Boston, Little, Brown and company, 75-77.

Gray, R., Leese, M., Bindman, J., Becker, T., Burti, L., David, A., Gournay, K., Kikkert, M., Koeter, M., Puschner, B., Schene, A., Thornicroft, G., & Tansella, M. (2006). Adherence therapy for people with schizophrenia. *British Journal of Psychiatry, 189*, 508-514.

Gray, R., Wykes, T., & Gournay, K. (2000). From compliance to concordance: a review of the literature on interventions to enhance compliance with antipsychotic medication. *Journal of Psychiatric and Mental Health Nursing*. *9*, 277-284.

Hayward, P. & Chan, N. (1995). Medication self-management; a preliminary report on an intervention to improve medication adherence. *Journal of Mental Health*, *4*, 511-17.

Hettema, J., Steele, J., & Miller, W. (2005). Motivational interviewing. Annual Review of Clinical Psychology, *1*, 91–111.

Hogan, T., Awad, A., & Eastwood, R. (1983). A self-report scale predictive of drug compliance in schizophrenics: reliability and discriminative validity. *Psychological Medicine*, *13*,177-183.

Hollis, C. (2000). Adult outcomes of child- and adolescent-onset schizophrenia: diagnostic stability and predictive validity. *American Journal of Psychiatry*, *157*, 1652-1659.

Howes, O., McDonald, C., Cannon, M., Arseneault, L., Boydell, J., & Murray, R. (2004). Pathways to schizophrenia: the impact of environmental factors. *International Journal of Neuropsychopharmacology*, *7* Suppl 1:S7-S13.

Jeste, D., Rockwell, E., Harris, M., Lohr, J., & Lacro, J. (1999). Conventional vs. newer antipsychotics in elderly patients. *American Journal of Geriatric Psychiatry*, *7*, *70*-76.

Jeste, D., Lacro, J., Bailey, A., Rockwell, E., Harris, M., & Caleguir, M. (1999). Lower incidence of tardive dyskinesia with risperidone compared with haloperidol in older patients. *Journal of the American Geriatrics Society*, *47*, 716-719.

Johnson, D., Paterski, G., Ludlow, J., Street, K., & Taylor, R. (1983). The discontinuance of maintenance neuroleptic therapy in chronic schizophrenic patients: drug and social consequences. *Acta Psychiatrica Scandinavica*, *67*, 339-352.

Kane, J. (1996). Schizophrenia. *New England Journal of Medicine*, *334*, 34-41.

Kelleher, J., Centorrino, F., Albert, M., & Baldessarini, R. (2002). Advances in atypical antipsychotics for the treatment of schizophrenia: new formulations and new agents. *CNS Drugs 2002*, *16*, 249-261.

Kemp, R., David, A., & Hayward, P. (1996). Compliance therapy: An intervention targeting insight and treatment adherence in psychotic patients**.** *Behavioural and Cognitive Psychotherapy, 24*, 331-350.

Kemp, R., Hayward, P., & David, A. (1997). Compliance therapy manual. *The Maudsley*, London.

Kemp, R., Kirov, G., Everitt, B., Hayward, P., & David, A. (1998). Randomised controlled trial of compliance therapy: 18-month follow-up. *British Journal of Psychiatry,172*, 413-419.

Keshavan, MS. (2005). First-episode schizophrenia: Research perspectives and clinical implications. *Psychiatric Times*, *22*, 3, 167-172.

Keshavan, MS., Anderson, S., & Pettegrew, JW. (1994). Is schizophrenia due to excessive pruning in the prefrontal cortex? The Feinburg hypothesis revisited. *Journal of Psychiatric Research*, *28*, 239-265.

Keshavan, MS., & Schooler, NR. (1992). First-episode studies in schizophrenia: criteria and characterization. *Schizophrenic Bulletin*,*18*, 491-513.

Kiene SM, Barta WD. (2006). A Brief Individualized Computer-Delivered Sexual Risk Reduction Intervention Increases HIV/AIDS Preventive Behavior. *Journal of Adolescent Health. 39*, 3, 404-410.

Kleist, K. (1960). Schizophrenic symptoms and cerebral pathology. *Journal of Mental Science*, *106*, 246-55.

Kurtz, M., Seltzer, J., Shagan, D., Thime, W., & Wexler, B. (2007). Computer-assisted cognitive remediation in schizophrenia: What is the active ingredient? *Schizophrenia Research 89*, 251–260.

Lacro, J., Dunn, L., Dolder, C., Leckband, S., & Jeste, D. (2002). Prevalence of and risk factors for medication nonadherence in patients with schizophrenia: a comprehensive review of recent literature. *Journal of Clinical Psychiatry*, *63*, 892-909.

Lawrie, SM. & Abukmeil, SS. (1998). Brain abnormality in schizophrenia: a systematic and quantitative review of volumetric magnetic resonance imaging studies. *British Journal of Psychiatry*, *172*, 110-120.

Lecompte, D. & Pelc, I. (1996). A cognitive-behavioral program to improve compliance with medication in patients with schizophrenia. *International Journal of Mental Health 25*, 51-56.

Leonhard, K., (1957). [Cycloid psychoses, often erroneously considered as schizophrenia.] Article in German. *Psychiatrie, Neurologie und Medizinische Psychologie*, *9*, 12, 359-65.

Lewis, DA., Lieberman, JA. (2000). Catching up on schizophrenia: Natural history and neurobiology. *Neuron, 28*, 325-334.

Lieberman, J., Perkins, D., Belger, A., Chakos, M., Jarskog, F., Boteva, K. & Gilmore, J. (2001). The early stages of schizophrenia: Speculations on pathogenesis, pathophysiology, and therapeutic approaches. *Biological Psychiatry 50*, 884-897.

MacKinnon, D. P., Lockwood, C. M., Hoffman, J. M.,West, S. G., & Sheets, V. (2002). A comparison of methods to test mediation and other intervening variable effects. *Psychological Methods*, *7*, 83–104.

Macpherson, R., Jerrom, B., & Hughes, A. (1996a). A controlled study of education about drug treatment in schizophrenia. *British Journal of Psychiatry*. *168*, 718-722.

Marder, S. & Meibach, R. (1994). Risperidone in the treatment of schizophrenia. *American Journal of Psychiatry*, *151*, 6, 825-835.

Markland, D., Ryan, R., Tobin, V., & Rollnick, S. (2005). Motivational interviewing and self-determination theory. *Journal of Social and Clinical Psychology, 24*, 811-831.

McClellan, J., McCurry, C., Speltz, M., & Jones, K. (2002). Symptom factors in early-onset psychotic disorders. *Journal of American Academy of Child and Adolescent Psychiatry*, *41*, 7, 791-8.

McConatha, J., McConatha, D., Deaner, S., & Dermigny, R. (1995). A computer-based intervention for the education and therapy of institutionalized older adults. *Educational Gerontology, 21*, 2, 129-138.

McIntosh, A., Conlon, L., Lawrie, S., & Stanfield, A. (2007). Compliance therapy for schizophrenia. *The Cochrane Collaboration*, John Wiley & Sons, Ltd.

Meehl, P. (1962). Schizotaxia, schizotypy, schizophrenia. *American Psychologist*, *17*, 827-838.

Mellor, C. (1982). The present status of first-rank symptoms. *British journal of Psychiatry*, *140*, 423-424.

Miller, W., & Rollnick, S. (1991). Motivational interviewing: preparing people to change. New York: Guilford Press.

Morisky, D., Green, L., & Levine, D. (1986). Concurrent and predictive validity of a self-reported measure of medication adherence. *Medical Care*, 24, 1, 67-74.

Murray, R. & Lewis, S. (1987). Is schizophrenia a neurodevelopmental disorder? *British Medical Journal 295*, 681-682.

Neighbors, C., Larimer, M., Lewis, M. (2004). Targeting misperceptions of descriptive drinking norms: efficacy of a computer-delivered personalized normative feedback intervention. *Journal of Consulting and Clinical Psychology, 72*, 3, 434-447.

Nose, M., Barbui, C., & Tansella, M. (2003). How often do patients with psychosis fail to adhere to treatment programmes? A systematic review. *Psychological Medicine*, *33*, 1149–1160.

O'Donnell, C., Donohoe, G., Sharkey, L., Owens, N., Migone, M., Harries, R., Kinsella, A., Larkin, C., & O'Callaghan, E. (2003). Compliance therapy: a randomised controlled trial in schizophrenia. *British Medical Journal* , *327,* 7419, 1-4.

Ondersma, S., Chase, S., Svikis, D., & Schuster, C. (2005). Computer-based brief motivational intervention for perinatal drug use. *Journal of Substance Abuse Treatment, 28*, 4, 305-312.

Ondersma, S., Svikis, D., & Schuster, C. (2007). Computer-Based Brief Intervention: A Randomized Trial with Postpartum Women. *American Journal of Preventive Medicine, 32*, 3, 231-238.

Overall, J., & Gorham, D. (1988). The brief psychiatric rating scale (BPRS): Recent developments in ascertainment and scaling. *Psychopharmacology Bulletin*, *24*, 97-99.

Roberto, C., Anselmetti, S., Poletti, S., Bechi, M., Ermoli, E., Cocchi, F., Stratta, P., Vita, A., Rossi, A., & Smeraldi, E. (2009). Computer-aided neurocognitive remediation as an enhancing strategy for schizophrenia rehabilitation. *Psychiatry Research*, *169*, 191–196.

Robinson, D., Woerner, M., Alvir, J., Bilder, R., Goldman, R., Geisler, S., Koreen, A., Sheitman, B., Chakos, M., Mayerhoff, D., & Lieberman, J. (1999). Predictors of relapse following response from a first episode of schizophrenia or schizoaffective disorder. *Archives of General Psychiatry*, *56*, 3, 241-247.

Robinson, D., Woerner, M., Alvir, J., Bilder, R., Hinrichsen, G., & Lieberman, J. (2002). Predictors of medication discontinuation by patients with first-episode schizophrenia and schizoaffective disorder. *Schizophrenia Research*, *57*, 2-3, 209-219.

Rohsenow, D. J., Monti, P. M., Martin, R. A., Colby, S., Myers, M., Gulliver, S., Brown, R., Mueller, T., Gordon, A., & Abrams, D. (2004). Motivational enhancement and coping skills training for cocaine abusers: effects on substance use outcomes. *Addiction*, *99*, 862–874.

Rossum, JM van. (1963). The relation between chemical structure and biological activity. *Journal of Pharmacy and Pharmacology*, *15*, 285-316.

Rossum, JM van. (1964). Significance of dopamine in psychomotor stimulant action. In: Trabucchi, E., Paoletti, R., Canal, N. eds., *Biochemical and Neurophysiological Correlation of Centrally Acting Drugs*. Oxford, Pergamon Press, 115-126.

Rossum, JM van. (1966). The significance for dopamine receptor blockade for the action of neuroleptics drugs. In: Brill, H., ed., *Neuro-psycho-pharmacology*. Amsterdam, Excerpta Medica foundation. 321-329.

Rubak, S., Sandboek, A., Lauritzen, T., & Christensen, B. (2005). Motivational Interviewing: a systematic review and meta-analysis. *British Journal of General Practice*, *55,* 305-312.

Schneider, K. (1957). [Primary & secondary symptoms in schizophrenia.] Article in German*. Fortschritte der Neurologie-Psychiatrie*, *25*, 9, 487-490.

Shadish, W., Hu, X., Glaser, R., Kownacki, R., & Wong, S. (1998). A method for exploring the effects of attrition in randomized experiments with dichotomous outcomes. *Psychological Methods, 3*, 1, 3-22.

Shifman, S., Bronstein, M., Sternfeld, M., Pisante-Shalom, A., Lev-Lehman, E., Weizman, A., Reznik, I., Spivak, B., Grisaru, N., Karp, L., Schiffer, R., Kotler, M., Stous, R., Swartz-Vanetik, M., Knobler, H., Shinar, E., Beckmann, J., Yakir, B., Risch, N., Zak, N., & Darvasi, A. (2002). A highly significant association between a COMT haplotype and schizophrenia. *American Journal of Human Genetics*, *71*, 1296-1302.

Shorter, E., (1997). *A History of Psychiatry*. Wiley, New York, pp.26-28, 93-99, 196-200.

Small, J., Hirsch, S., Arvanitis, L., Miller, B., & Link, C. (1997). Quetiapine in patients with schizophrenia. A high- and low-dose double-blind comparison with placebo. Seroquel Study Group. *Archives of General Psychiatry*, 54, 6, 549-557.

Smeeth, L., & Ebrahim, S. (2000). Commentary: DINS, PINS, and things--clinical and population perspectives on treatment effects. *British Medical Journal, 321*, 952-953.

Smith, J., Birchwood, M., & Haddrell, A. (1992). Informing people with schizophrenia about their illness: The effect of residual symptoms. *Journal of Mental Health*, *1*, 61-70.

Sobell, L., Sobell, M., & Agrawal, S. (2009). Randomized Controlled Trial of a Cognitive–Behavioral Motivational Intervention in a Group Versus Individual Format for Substance Use Disorders. *Psychology of Addictive Behaviors,* Vol. *23*, 4, 672–683.

Stefansson, H., Steinhorsdottir, V., Thorgeirsson, T., Gulcher, J., & Stefansson, K. (2004). Neuregulin 1 and schizophrenia. *Annals of Medicine*, *36*, 1, 62-71.

Steinberg, M., Ziedonis, D., Krejci, J., & Brandon, T. (2004). Motivational interviewing with personalized feedback: A brief intervention for motivating smokers with schizophrenia to seek treatment for tobacco dependence. *Journal of Consulting and Clinical Psychology, 72*, 4, 723-728.

Stotts A. L., Schmitz J. M., Rhoades H. M., Grabowski J. (2001). Motivational interviewing with cocaine-dependent patients: a pilot study. *Journal of Consulting and Clinical Psychology*, *69*, 5, 858-862.

Streicker, S., Amdur, M., & Dincin, J. (1986). Educating patients about psychiatric medication: failure to enhance compliance. *Psychosocial Rehabilitation*, *4*, 15-28.

Thompson, K., Kulkarni, J., & Sergejew, A. (2000). Reliability and validity of a new Medication Adherence Rating Scale (MARS) for the psychoses. *Schizophrenia Research*, *42*, 3, 241-247.

Tollefson, G., Beasley, C., Tamura, R., Tran, P., & Potvin, J. (1997). Blind, controlled, long-term study of the comparative incidence of treatment-emergent tardive dyskinesia with olanzapine or haloperidol. *American Journal of Psychiatry*, *154*, 9, 1248-1254.

Van Putten, T., May, P., Marder, S. (1984). Response to antipsychotic medication: the doctor's and the consumer's view. *American Journal of Psychiatry 141,* 16-19.

Vansteenkiste, M., & Sheldon, K. (2006). There's nothing more practical than a good theory: Integrating motivational interviewing and self-determination theory. *British Journal of Clinical Psychology, 45*, 63-82

Weinberger, DR. (1987). Implications of normal brain development for the pathogenesis of schizophrenia. *Archives of General Psychiatry 44*, 660-669.

Weissman, M. & Bothwell, S. (1976). Assessment of social adjustment by patient self-report. *Archives of General Psychiatry, 33*, 9, 1111-1115.

Woodruff, P., McManus, I. & David, AS. (1995). Meta-analysis of corpus callosum size in schizophrenia. *Journal of Neurological and Neurosurgical Psychiatry*, *58*, 457-461.

Woolley, DW. & Shaw, E. (1954). A biochemical and pharmacological suggestion about certain mental disorders. *Proceedings of the National Academy of Sciences 40*, 228-231.

Wright, I., Rabe-Hesketh, S., Woodruff, P., David, A., Murray, R. & Bullmore, E. (2000). Meta-analysis of regional brain volumes in schizophrenia. *American Journal of Psychiatry*, *157*, 1, 16-21

Zubin, J. & Spring, B. (1977). Vulnerability-a new view of schizophrenia. *Journal of Abnormal Psychology*, *86*, 103-126.

ABSTRACT

COMPUTER-BASED BRIEF MOTIVATIONAL INTERVENTION FOR MEDICATION ADHERENCE IN SCHIZOPHRENIA

by

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Major: Psychology

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Despite the documented efficacy of medication treatments for individuals suffering from schizophrenia, many individuals suffering from this disorder are unable or unwilling to adhere to their medication regimen. This may be due to the inability of providers to differentially address the individual motivation levels of their patients. The few interventions that have shown promise are both costly and difficult to disseminate. The current study is a randomized controlled trial which utilizes motivational interviewing, delivered with an interactive computer based delivery system to address attitudes about adherence. Feasibility, acceptability and efficacy were examined as outcomes. While both feasibility and efficacy were shown to be strong indicators that this is a viable way to reach this population, there was no significant increase in attitudes surrounding adherence.

AUTOBIOGRAPHICAL STATEMENT

Robert Kender is a native of Flint, Michigan and did his undergraduate work in psychology and philosophy at the University of Michigan – Flint. He did his Master's degree at Wayne State University in a biopsychology laboratory before completing his Ph.D. in clinical psychology. He currently resides in Dearborn, Michigan.