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Emerging Behavioral and Psychotherapeutic Interventions for Schizophrenia

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INTRODUCTION

Since the introduction of typical antipsychotic medications in the 1950s and subsequent development of novel or atypical antipsychotic medications in the 1990s, pharmacological treatment has been central to the management of schizophrenia (1,2). Both typical and novel antipsychotic medications decrease hallucinations and delusions in patients, and reduce relapse rates compared to placebo. A meta-analysis of 65 trials demonstrated that antipsychotic drugs reduced relapse rates at one year (27%) compared to placebo (64%), with evidence also suggesting better quality of life, and fewer aggressive behaviors in treated patients (3). Nevertheless, the long term course of schizophrenia remains disappointing, with only a minority of patients sustaining high levels of psychosocial and occupational function after the first episode of illness. Hegarty conducted a meta-analysis of the pre- and post-chlorpromazine era (1895 to 1992) comparing outcomes at an average of 5.6 years of follow-up (4). Improvement was defined as recovery with minimal to mild clinical symptoms and good psychosocial functioning as indicated by work or independent living. Hegarty found that the proportion of patients diagnosed with narrow criteria (at least six months of illness) who improved increased after the mid-20th century from 35% to 48%, suggesting that while antipsychotic medication had a modest positive effect on long term outcomes, many patients still failed to show good recovery. A more recent meta-analysis applied a definition of recovery that required both clinical remission and good social functioning that persisted at least two years and included studies from the novel antipsychotic period (5). Using the criteria of sustained clinical and psychosocial recovery, the median proportion of patients who met recovery criteria was only 14%. The recovery rates did not differ by gender, duration of follow-up, time of data collection or strictness of diagnostic criteria. Because the onset of schizophrenia is typically early in adulthood, the disability and diminished quality of life in the disorder takes an enormous toll on affected individuals and caregivers. Moreover, schizophrenia is associated with a 2 to 3-fold increase in mortality rates compared to the general population (6) with life expectancy reduced up to two decades (7-9). Common causes of death include cardiovascular mortality,

cancer mortality, chronic obstructive pulmonary disease, influenza and pneumonia, substance-induced death, accidental death and suicide (10,11). Factors that likely contribute to increased mortality in schizophrenia include tobacco smoking, alcohol dependence or addiction, obesity, lack of adequate medical care, lack of medical compliance and sedentary life style. Side effects of some novel antipsychotic medications, such as weight gain, may also play a role in increased risk for metabolic syndrome (12,13).

Appreciation of the poor psychosocial outcomes, degraded quality of life and premature mortality in schizophrenia has spurred interest in development of behavioral and psychotherapeutic interventions which complement pharmacological management, and improve these outcomes. We will review emerging non-pharmacological interventions for schizophrenia, and evaluate the state of evidence for clinical efficacy with an emphasis on randomized controlled trials (RCTs). Interventions under consideration include exercise, cognitive remediation, cognitive-behavior therapy, psychosocial interventions such as assertive community treatment, supported employment and family interventions. Clinical practice recommendations and future directions are also considered. Magnitude of effects are assessed with the effect size measures of Cohen's d and Hedges' g (14), odds ratios and hazard ratios.

Physical Activity and Exercise Interventions

Sedantary life style has been associated with elevated risk for development of increased morbidity and mortality in the general population. Sedentary behavior is characterized by a severe reduction in physical activity and energy expenditure which has been defined both by low energy expenditure (resting metabolic rate ≤1.5 metabolic equivalents) and a sitting or reclining posture (15). A recent meta-analysis indicated associations between sedentary life style and all-cause mortality (Hazard ratio [HR]:1.24), cardiovascular disease mortality (HR:1.17), cancer mortality (HR:1.17) and type 2 diabetes incidence (HR:1.91) (16). Notably, these illness outcomes are all elevated in schizophrenia. Persons with schizophrenia engage in less vigorous physical activity per day than healthy adults, but do engage in comparable levels of light physical activity, nearly 90 minutes per day (17). This may be due to the finding that walking is the primary means of transit for most persons with schizophrenia, and walking is a form of light exercise. Nevertheless, a meta-analysis demonstrated that patients with psychotic disorders spend greater amounts of their day in sedentary behavior compared to control subjects (g=1.13), a difference of about 2.8 hours per day (18). Studies with objective measures of sedentary behavior, rather than self-report questionnaires, suggested that patients spent at least 12.5 hours of their day-time in a sedentary life style. It is likely that greater levels of sedentary behavior contribute to elevated risks for cardiovascular disease, obesity, cancer and diabetes observed in individuals with schizophrenia and other psychotic disorders.

Interventions to increase levels of physical activity, particularly moderate to intense exercise, could diminish the morbidity and mortality associated with sedentary life style observed in schizophrenia. Moreover, recent trials in patients with schizophrenia provide evidence that increased unstructured physical activity or exercise programs can also improve neurocognitive function. In a review and meta-analysis, Firth et al. (19) evaluated ten articles with 385 subjects in whom exercise interventions, defined as structured and repetitive physical activity were tested to improve or maintain physical fitness, on cognitive function in persons with non-affective psychotic disorders. Exercise improved global cognition (g=0.33) with specific effects on working memory (g=0.39), attention/vigilance (g=0.66) and social cognition (g=0.71). In contrast, effect sizes for processing speed, verbal learning, visual learning and problem solving were not significant, suggesting that aerobic exercise may be beneficial for some cognitive domains more than others. Minutes of exercise per week approached significance as a moderator variable, and were consistent with the dose effect. Notably, a significant effect on global cognition was observed when exercise was managed by physical activity professionals rather

than by mental health staff. In contrast to exercise effects on cognition, surprisingly few studies have evaluated the effects of exercise on cardiovascular fitness or weight in schizophrenia. These have been largely negative outcomes (20), mirroring the difficulty in using exercise for sustained weight loss in non-psychiatric populations (21). In a meta-analysis of eight RCTs comparing exercise to usual care, there were no effects on negative symptoms, positive symptoms, depression, anxiety or body weight (22). Thus, it is possible that exercise may have significant effects on cognition in schizophrenia even in the absence of clinically meaningful effects on psychiatric symptoms, cardiovascular system or weight.

The biological mechanisms associated with exercise that ameliorate cognitive deficits in persons with schizophrenia are still little understood. Rodent studies have shown that physical activity and exercise enhance performance on a wide range of tasks, including spatial learning and memory, fear conditioning, passive avoidance learning and novel object recognition (23). A diversity of biological mechanisms may contribute to these behavioral improvements. Exercise increases brain derived neurotrophic factor (BDNF) expression in the brain. In mice, increased BDNF expression in brain results from action of a ketone, β-hydroxybutyrate, which is produced by the liver after prolonged exercise. In rodents, exercise increases neurogenesis, synaptic plasticity and dendritic spine density (23). Exercise suppresses neuroinflammation, which has been implicated in the pathogenesis of schizophrenia (24,25). Thus, animal models support both neurotrophic and neuroprotective effects of exercise on the brain, although these have yet to been directly demonstrated in the central nervous system of individuals with schizophrenia.

While preclinical studies suggest that physical activity and exercise appear to have great potential as an adjunctive intervention in schizophrenia, the small number of RCTs utilizing this approach are not yet adequate to provide guidelines for optimal intensity, frequency or type of exercise for clinical implementation. Exercise effects have been most clearly demonstrated for general cognition, but it is possible that specific exercise regimens could also affect mood or psychotic symptoms. Incorporation of biological measures such as peripheral levels of ketones and MRI measures of responses in brain structure, function and metabolites can characterize mechanisms producing cognitive change. Finally, increasing physical activity and exercise levels in clinical populations are challenging, and require well-designed protocols to maintain adherence (26-28).

Cognitive Remediation

Schizophrenia is associated with pervasive cognitive impairment which encompasses perception, attention, processing speed, working memory, learning, social cognition and motor control (29,30). In patients, measures of global cognitive performance or intelligence are reduced about two thirds of a standard deviation from those of gender- and age-matched non-psychiatric groups. Longitudinal studies have shown that cognitive deficits are present in childhood. Some deficits may worsen over childhood and adolescence, such as working memory and processing speed (31). Further decline may occur in the course of the first episode of psychosis with little further change thereafter (30). Cognitive function is associated with current functional level, and contributes to long term functional outcomes (32,33). Unfortunately, antipsychotic medications typically do not produce a significant improvement in cognitive performance and effective pharmacological agents for improving cognition have not been developed yet (34).

While schizophrenia is associated with impaired learning performance, individuals affected by the illness retain the capacity for learning and adaptation. In a cognitive remediation application, a person engages in activities designed to improve specific cognitive processes, such as auditory attention, visual working memory or learning and memory. Over the past decade, there was a keen interest in behavioral activities which could produce significant and sustained improvement in cognitive function and adaptive behavior in community settings, with development and commercialization of computer

based training software. Computer based training has many advantages, including standardized task administration, on-line response monitoring and feedback, adaptive levels of task difficulty which adjust to a user's performance level, game-like design and ease of administration by clinical staff or caregivers. Many approaches have been used in the design of cognitive remediation. For example, in working memory training, Morrison and Chein (35) differentiated two types of training approaches in the literature, strategy training and core training. Strategy training emphasizes the use of domain-specific strategies to assist with encoding, maintenance or retrieval in improving working memory performance on training tasks. Core strategy training usually requires extensive repetition of a broad range of working memory tasks which vary in stimulus characteristics and task demands. Morrison and Chein (35) concluded that both tasks resulted in training-related increases in working memory performance, but the core approach appeared to foster broader transfer effects to other types of cognitive tasks. The range of variations in approach presents a challenge in evaluating evidence for efficacy, since studies vary in the domains of cognition targeted, the duration and frequency of practice sessions, the types of stimuli and level of difficulty and overall duration of the intervention. A major distinction in evaluating outcomes of training is whether generalization or transfer of training occurs. Transfer may be near, in which performance improves for tasks similar to those used in training, or far, in which performance is improved for tasks of functions that are not obviously related to training targets. In the case of working memory training, meta-analysis suggests that near-transfer can occur for a range of working memory tasks after training. However, there is little evidence that such training improves other cognitive skills such as verbal ability or arithmetic (36).

Patients with schizophrenia can improve skills on a variety of tasks with practice, and near-transfer to tasks similar to the training task can occur (37). However, a meaningful clinical intervention would require that effects of cognitive remediation generalize to a broad range of cognitive domains, improve cognitive performance and problem solving in everyday life and have enduring effects. With respect to generalization of cognitive training to measures of general cognition, several meta-analytic studies have been encouraging. Wykes et al. (38) carried out a meta-analysis of 40 studies published up to 2009, including trials in which group comparisons were performed, and tested outcome measures distinct from the trained tasks. The mean effect size (d) was 0.45 on global cognition and 0.43 on level of function. In contrast, there was no effect on psychiatric symptoms. A review focused on computer-assisted cognitive remediation showed a mean effect size of 0.38 for a variety of test measures. Revell et al. (39) reviewed 11 cognitive remediation trials for early schizophrenia published through 2015. The effect size on global cognition was non-significant (0.13), although there were small significant effects were found for global symptoms (0.19), and functioning (0.18). These reviews and analyses suggest that cognitive remediation may have a small to moderate effect size for improving measures of overall cognition with small to negligible effects on psychiatric symptoms. Moreover, effects may be attenuated in persons in the early stage of the illness.

A concern in assessing efficacy of cognitive remediation is the frequency of design weaknesses in the literature. In the Wykes et al. (38) meta-analysis, underpowered sample sizes (60%), lack of independent randomization (70%), lack of treatment fidelity assessment (80%), and lack of allocation masking (73%) were frequently observed. In the Grynszpan et al. (40) meta-analysis, 63% of the studies use a treatment-as-usual (TUA) control arm, which fails to control for the non-specific effects of the activities involved in participating in a cognitive remediation study. Revell et al. (39) found a much larger effect of cognitive remediation in open label trials (0.54) compared to blinded ones (0.08). Most perplexing for clinical service providers is the bewildering heterogeneity of intervention modalities, treatment schedules and durations under consideration. Nevertheless, the results from cognitive remediation are more promising than any pharmacological

cognitive enhancer currently available and are not associated with known adverse effects. Increasing recognition of the importance of rigorous study design, and incorporation of psychosocial outcomes such as employment will help clarify the clinical utility of these interventions (41-43).

Cognitive Behavior Therapy for Psychosis

Cognitive behavioral therapy for psychosis (CBTp) was adapted from cognitive behavioral therapy (CBT). CBT is based on the principles which were developed by Beck (1970) and Ellis (1962), and focused on the role of maladaptive thoughts in the production and maintenance of emotional distress, and problematic behaviors (44,45). CBT is a talk therapy to help consumers discern the relationship between their thoughts, feelings and behaviors with the aim to restructure negative cognitions and decrease self-destructive behavior. Uniquely from other psychological interventions for psychosis, CBTp focuses on challenging delusions, normalizing psychotic experience, and determining the onset of psychotic symptoms from the perspective of a stress vulnerability model (46).

With accumulating evidence regarding the effectiveness of CBTp, national guidelines in the United Kingdom (47,48), United States (49), Canada (50), Sweden (51), and Scotland (52) recommend CBTp for the treatment of symptoms of schizophrenia. Nevertheless, at least seventeen meta-analyses conducted in the last decade, and half of them revealed inconsistent findings regarding the efficacy of CBTp. Meta-analyses indicated small to large effect sizes ranging from 0.21 to 1.31 for positive symptoms (53-61), 0.21 to 1.08 for negative symptoms (56,57,59,61), and from 0.21 (in favor of CBTp) to 0.65 for general psychopathology (53,57,61,62). However, several recent meta-analyses have suggested that CBTp has no significant effect on positive or negative symptoms, or overall psychopathology (g<0.2) (63-65).

The discrepancies between meta-analytic findings may be due to the variation of studies included in analysis. As depicted by Jauhar et al. (61), there were marked differences in effect sizes when studies were re-categorized according to risk for bias from insufficient sequence generation, allocation concealment, and masking, as well as from incomplete outcome data. For example, studies at low risk for allocation concealment, indicating that randomization was performed independent of investigators, showed small effect sizes for positive symptom improvement after CBTp (g=-0.19, in factor of CBTp), while those at high risk for bias from unclear or no allocation concealment showed moderate-large effect sizes (g=-0.96, in favor of CBTp). The inclusion of clearly randomized control trials versus quasi-experimental designs also appears to have contributed to variations in effect sizes, thus suggesting that effectiveness of CBTp may be associated with quality of study (63,66).

CBTp has also been criticized for having limited effective implementation possibly due to long duration of standard treatment, which requires approximately 12 sessions (average 16-20 sessions) over 6-9 months. A recent meta-analysis, however, of nine articles covering seven studies, and 1207 participants demonstrated that a brief version of CBTp, administered in 6-10 sessions over a 4 month period might also be effective (67). Compared to treatment as usual, brief CBTp had medium effect sizes (g=0.43), and showed a small effect compared to other treatments (g=0.38) and moderate effect sizes for the treatment of positive symptoms (g=0.48) such as delusions (g=0.56) and hallucinations (g=0.45), as well as negative symptoms (g=0.90) (67). Additionally, this meta-analysis also found small to moderate improvement in anxiety, depression, distress, insight and quality of life. Importantly, many of these improvements remained 3-6 months after the termination of treatment (67). A second meta-analysis evaluated ten studies which utilized low intensity CBTp administered over 6-15 sessions. The results were also promising in that brief CBTp generated improvement in symptoms of psychosis at the conclusion of treatment which were still apparent after 3-18 months of follow-up (d=-0.40) (68). At follow-up, participants also showed significant improvement

in depression and functioning (d=-0.56 and d=-0.57 in favor of CBTp, respectively). Importantly, study quality, the number of hours and/or sessions of therapist contact, and individual versus group format were not significant moderators of improvement. Taken together, these meta-analyses suggest that brief CBTp has exciting therapeutic potential in schizophrenia.

Part of the discord between meta-analyses may also be due to the fact that while CBTp has common elements across approaches (e.g. modifying maladaptive beliefs and delusions) there is a wide heterogeneity of delivered content, techniques, outcome measures and patient characteristics. Additionally, in part due to the variation of techniques, little is currently known about mechanisms of change associated with the intervention. Recent neuroimaging research, however, found that CBTp, compared to treatment as usual, generated clinical improvement and decreased neural activation in regions of the brain associated with distress, such as the inferior frontal, insula, thalamus, putamen and occipital areas (69). The results suggested that CBTp might be effective by decreasing distress associated with threat (69). Further neuroimaging investigations have also implicated individual differences predicting responsiveness to CBTp. Kumari et al. (70) revealed that changes in activation in regions responsible for language processing, attention, insight and self-awareness were associated with symptom improvement. Premkumar et al. (71) demonstrated that increased gray matter in the orbitofrontal cortex, a region associated with impulsivity and emotional decision making, was also associated with response to CBTp. Increases in the anterior cingulate cortex (ACC) of a metabolite associated with mitochondrial and NMDA receptor function as well as neuronal longevity known as N-acetyl aspartate (NAA) were also associated with symptom improvement after CBTp (72).

While there are discrepancies between meta-analyses examining the efficacy of CBTp for schizophrenia, there appears to be promising evidence that CBTp is effective in decreasing the overall symptoms of schizophrenia, and that CBTp remains effective when implemented over a brief or limited duration. There is also growing evidence of neurobiological change associated with improvement in symptoms as a result of CBTp. Significantly, CBTp was not shown to be any worse than other psychological treatments. Therefore, clients with schizophrenia have the potential to benefit from CBTp. Further research is warned to discern 1) the mechanism of change associated with CBTp, 2) the important and critical components of treatment, and 3) individual differences associated with CBTp's effectiveness.

Psychosocial Interventions

Psychosocial interventions broadly aim to increase quality of life, and improve individual and social functioning through social integration interventions. While there have been several proposed psychosocial interventions, there is significant empirical support for team-based care, vocational rehabilitation through supported employment as well as family interventions. Support for psychosocial interventions comes from multiple RCTs, meta-analyses and subsequent national guidelines from the United States (49) and Germany (73).

Assertive Community Treatment (ACT)

Assertive community treatment (ACT) was designed to help increase access to mental health services for those with severe mental illness and frequent hospitalizations, legal problems, homelessness and/or substance abuse problems (74). ACT involves an interdisciplinary team, often consisting of a psychiatrist or medication prescriber, psychologist, nurse, and other uniquely required specialists such as a vocational rehabilitation specialist (75). Also, ACT has a low client-staff ratio of approximately ten clients per team, and treatment is not time-limited. ACT teams meet daily to discuss treatment planning, with each specialist contributing their expertise as needed (75).

Coldwell and Bender (76) demonstrated ACT's efficacy in a meta-analysis of ten studies and 5,775 participants.

Investigators reported that in RCTs, ACT produced a 37% decrease in homelessness ($p<0.0001$) and 26% improvement in psychiatric symptoms ($p=0.006$). Compared to baseline levels, observational studies also showed a significant decrease in rates of homelessness and psychiatric symptoms ($p\leq0.05$). These results suggest that ACT is superior to traditional case management in reducing rates of homelessness and psychiatric symptoms. Given the support for the efficacy of ACT programs some national guidelines recommend the use of an assertive, multidisciplinary psychiatric community care team for the treatment of severe mental illness, in particular for homeless individuals (49,73).

Of note, while studies outside of the United States have indicated that ACT was effective in maintaining communication with difficult to engage individuals, some studies in the United Kingdom failed to replicate previously observed benefits, such as decreases in psychiatric symptoms, functional improvement, and decreased inpatient stays (77,78). These studies suggest that ACT may be less beneficial in communities where standard treatment already involves components of ACT, as was the case in the United Kingdom and likely why ACT showed no improvement compared to standard of care control conditions.

Overall, ACT appears to be beneficial for consumers in helping decrease rates of homelessness and psychotic symptoms. Additionally, ACT would be appropriate and recommended for communities in which standard treatment fails to incorporate ACT-like approaches to care.

Supported Employment

Even though many persons with schizophrenia want to work (79), employment rates are much lower than in the general population in the United State and Europe (80,81). Also, those with severe mental illness have difficulty in maintaining employment due to stigma, educational disadvantages, and chronic and/or acute mental health symptoms (82). Supported employment (SE) involves getting individuals into a competitive job while concurrently providing support to maintain employment. One of the forms of SE with the best empirical support is the individual placement and support (IPS) program (83). IPS requires that participants want competitive employment, and involves a rapid job search, respect for client decisions regarding job preferences and whether or not to share psychiatric history with employer, followed by simultaneous support for job development, integration of both vocational and clinical services, and benefits counseling. Also, IPS is not time-limited.

Meta-analyses have consistently reported that IPS SE would be more successful in aiding individuals in finding competitive employment compared to traditional vocational rehabilitation approaches, with effect sizes ranging from 0.77 to 0.96 (84,85). These results were supported by a meta-analysis, and review which also indicated that those who participated in IPS were twice as likely to gain competitive employment compared to others treated with traditional vocational rehabilitation (82), and that SE increased hours and weeks worked as well as wages (86).

SE may also have non-vocational benefits. In addition to financial gain (87), with employment, previously unemployed individuals have shown decreased psychiatric hospitalizations (88) and outpatient psychiatric services (89), fewer days hospitalized, decreased positive and negative symptoms (90), and increased in self-esteem (89). Importantly, employment was not related to worsening of outcomes (89) and evidence of lasting benefit was observed as long as 5 years after participation in IPS SE (91). Also, demographic characteristics, and psychiatric and employment history of consumers appeared to have little impact on the overall success of IPS SE (85).

Evidence supports that SE programs such as IPS have both vocational and potential non-vocational benefits. While non-vocational benefits appear promising, these are still a collection of individual studies, and thus further evaluation for consistency of findings is warranted. Collectively, these results suggest that competitive employment obtained through SE is likely beneficial to consumers with schizophrenia and further that benefit may be sustained long-term.

Family Interventions

As reviewed by Mueser et al. (83), even though many individuals with schizophrenia live at home, family members often have limited knowledge about the disease. This lack of knowledge can lead to increased stress and burden on the family, which has the potential to increase relapse. There are several variations of family interventions, but most commonly family psychoeducation consists of strategies to effectively work with a relative with schizophrenia, and to increase collaboration between family members and clinical care providers. Family psychoeducation typically reviews content about illness, medication and treatment management, coordination of services, problem solving, coping and rehabilitative services, and crisis planning, as well as discussion about expectations and distress, as well as social support (92).

Meta-analysis by Pilling et al. concluded that family interventions had potentially preventative effects on both relapse and re-hospitalization, with specific emphasis on single family therapy (93). With respect to relapse, investigators found effect sizes of 0.63 and 0.40 for effectiveness within 12 months of treatment, and after 1-2 years, respectively. Regarding re-hospitalization, Pilling et al. reported small to moderate effect sizes of 0.21 and 0.60, for within 12 months and 1-2 years, respectively, suggesting that family interventions might have long-term positive effect on re-hospitalization rates. Considering these findings, authors recommended that family interventions should be offered to families of those with schizophrenia. Several studies and subsequent reviews reported similar results (55,83,92,94,95). Support for family intervention also resulted in some national guideline recommendation that treatment would be offered to caregivers (49,73). While additional research is warranted to determine the necessary components and potential mediating and/or moderating factors of family interventions, it appears that offering family interventions to individuals with schizophrenia with involved caregivers would be beneficial to all parties.

Clinical Practice Recommendations and Future Directions

Clinical researchers have developed and tested a remarkable range of behavioral and psychotherapeutic interventions for schizophrenia. The evidence for several approaches is already compelling. There is rigorous empirical support for the efficacy of short term CBTp, and psychosocial interventions, such as supported employment and family interventions. Both effect sizes and other outcome measures indicate that these interventions have the potential to make a major difference in the lives of patients and caregivers, and to reduce economic burden of psychiatric disability. While cognitive remediation has been supported by several meta-analytic reviews, larger scale studies with systematic assessment of dose, task generalization, changes in everyday behavior, and individual differences in response are needed to establish standard implementations for dissemination. The striking procognitive and neurotrophic effects of physical activity in animal models has motivated preliminary studies of exercise based intervention for cognitive improvement in schizophrenia. Additionally, increased physical activity would likely improve health outcomes for patients with psychotic disorders. While clinical studies of exercise and activity interventions are very premature now, this approach is extremely promising.

In addition to the interventions considered in the present review, there are also promising novel treatment conceptualizations and delivery methods that warrant mention. For example, recently, the first meta-analysis on self-help interventions showed small to medium effect sizes on overall and positive symptoms (96). Interventions that utilize everyday technology, such as smartphones, have suggested that real-time illness management support may decrease symptoms of psychosis, depression and general psychopathology (97,98). Metacognitive therapy, which seeks to develop self-reflectivity, awareness of cognitive function of the self and others, and insight into illness may provide a psychotherapeutic technique for ameliorating the impact of delusional

and hallucinatory experiences (99,100).

It is likely that integration of multiple intervention methods, and targets will be the most effective approach to facilitating recovery from such a multidimensional disorder as schizophrenia. Even physical disorders with well characterized pathophysiology often require an integrated approach. For example, optimal management of Type II diabetes may require pharmacological treatment, education, dietary changes, exercise and self-monitoring of glucose levels (101). Similarly, Assertive Community Treatment of severe mental illness requires integration and communication among a diverse treatment team and client. Future research should consider integrative techniques which utilize critical components across interventions (102).

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