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Developing a Cognitive Training Strategy for First-Episode Schizophrenia: Integrating Bottom-Up and Top-Down Approaches

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Abstract

It is clear that people with schizophrenia typically have cognitive problems in multiple domains as part of their illness. The cognitive deficits are among the main contributors to limitations in their everyday functioning, including their work recovery. Cognitive remediation has been applied successfully to help people with long-term, persistent schizophrenia to improve their cognitive functioning, but it is only beginning to be applied with individuals who have recently had a first episode of psychosis. Several different approaches to cognitive training have been developed. Some approaches emphasize extensive systematic practice with lower-level cognitive processes and building toward higher-level processes ("bottom-up"), while others emphasize greater focus on high-level cognitive processes that normally integrate and organize lower-level processes ("top-down"). Each approach has advantages and disadvantages for a disorder like schizophrenia, with its multiple levels of cognitive dysfunction. In addition, approaches to cognitive remediation differ in the extent to which they systematically facilitate transfer of learning to everyday functioning. We describe in this article the cognitive training approach that was developed for a UCLA study of people with a recent first episode of schizophrenia, a group that may benefit greatly from early intervention that focuses on cognition and recovery of work functioning. This approach integrated bottom-up and top-down computerized cognitive training and incorporated an additional weekly group session to bridge between computerized training and application to everyday work and school functioning.

Introduction

The influence of Robert P. Liberman on the development of effective psychiatric rehabilitation is both broad and deep (Liberman, 1992, 1994, 2008; Liberman, Massel,

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Mosk, & Wong, 1985), as witnessed by the range of contributions in this festschrift in his honor. Nowhere has this influence been greater than at UCLA, where Bob Liberman developed and directed a NIMH-funded Clinical Research Center for the Study of Schizophrenia for 23 years from 1977 to 2000. He encouraged ongoing collaboration among clinical researchers, not only from his own areas of expertise in behavioral assessment, behavior therapy, social skills training, and psychiatric rehabilitation, but also with those who focused on cognitive deficits, psychophysiological abnormalities, and social and familial interactional processes in schizophrenia. His encouragement to bridge from the experimental psychopathology of cognition in schizophrenia to the evaluation of the promise of cognitive remediation was a key influence on the directions described in this article.

This article describes the background and development of a cognitive training approach for first-episode schizophrenia, drawing from the literature on cognitive deficits in schizophrenia, their links to functional outcome, and cognitive remediation approaches previously applied to chronic schizophrenia. This cognitive training approach was systematically evaluated in a recently completed randomized controlled trial at the UCLA Aftercare Research Program, the results of which will be reported in a later article. The general approach of teaching cognitive skills to individuals with schizophrenia, in this case through the use of computer software programs and cognitive coaches, is a fundamental part of a skills-based path to recovery advocated by Bob Liberman.

Cognitive Deficits Are Core Features of Schizophrenia

Cognitive deficits are now widely regarded as core, enduring features of schizophrenia. They are present not only during psychotic periods but also during clinical remission (Asarnow & MacCrimmon, 1982; Nuechterlein & Dawson, 1984; Nuechterlein, Dawson, Gitlin, Ventura, Goldstein, Snyder, Yee, & Mintz, 1992). In people with schizophrenia the severity of cognitive impairment is correlated very weakly, if at all, with level of concurrent delusions and hallucinations (Bilder, Goldman, Robinson, Reiter, Bell, Bates, Pappadopulos, Willson, Alvir, Woerner, Geisler, Kane, & Lieberman, 2000; Ventura, Thames, Wood, Guzik, & Hellemann, 2010). Furthermore, several studies indicate that cognitive deficits were often present years before the onset of schizophrenia or schizophrenia spectrum disorder (Cornblatt, Obuchowski, Roberts, Pollack, & Erlenmeyer-Kimling, 1999; Davidson, Reichenberg, Rabinowitz, Weiser, Kaplan, & Mark, 1999; Erlenmeyer-Kimling, Rock, Roberts, Janal, Kestenbaum, Cornblatt, Adamo, & Gottesman, 2000; Niendam, Bearden, Rosso, Sanchez, Hadley, Nuechterlein, & Cannon, 2003). The fact that first-degree relatives show an attenuated version of this pattern of cognitive deficits further indicates that cognitive deficits are not secondary to schizophrenic symptoms, but rather are likely to be influenced by genetic susceptibility factors (Asarnow, Nuechterlein, Subotnik, Fogelson, Torquato, & Payne, 2002; Gur, Calkins, Gur, Horan, Nuechterlein, Seidman, & Stone, 2007; Nuechterlein, Asarnow, Subotnik, Fogelson, Ventura, Torquato, & Dawson, 1998; Snitz, MacDonald, & Carter, 2006). In the absence of specific intervention attempts targeting cognitive deficits, the level of cognitive deficit in several domains tends to remain relatively stable over time in the initial years of illness (Finkelstein, Cannon, Gur, Gur, & Moberg, 1997; Hoff, Sakuma, Wieneke, Horon, Kushner, & DeLisi, 1999; Nopoulos, Flashman, Flaum, Arndt, & Andreasen, 1994).

A systematic review (Nuechterlein, Barch, Gold, Goldberg, Green, & Heaton, 2004) of all available factor analytic studies of cognitive performance in schizophrenia led to the conclusion that there are seven separable cognitive domains that could profit from intervention: processing speed, attention/vigilance, working memory, verbal learning, visual learning, reasoning and problem solving, and social cognition. All of these cognitive domains show large mean deficits in chronic schizophrenia, ranging from about 1 to almost 2 standard deviations below community subjects of similar age and gender, with processing speed and working memory being somewhat more impaired than other domains (R. S. Kern, Gold, Dickinson, Green, Nuechterlein, Baade, Keefe, Mesholam-Gately, Seidman, Lee, Sugar, & Marder, 2011).

Cognitive Deficits Are Linked to Functional Outcome in Schizophrenia

These core cognitive deficits have critical implications for everyday functioning in schizophrenia. Michael Green and colleagues summarized the evidence in three influential reviews (Green, 1996; Green, Kern, Braff, & Mintz, 2000; Green, Kern, & Heaton, 2004a) and a recent meta-analysis has confirmed their conclusions (Fett, Viechtbauer, Dominguez, Penn, van Os, & Krabbendam, 2011). Consistent and highly significant relationships with functional outcome were detected for several key cognitive domains, including verbal and visual learning and memory, immediate/working memory, processing speed, attention/vigilance, reasoning and problem solving, and social cognition (Fett, et al., 2011; Green, et al., 2000). Effect sizes were typically small to medium for individual cognitive measures, but sometimes large for composites across several cognitive domains.

The studies were initially cross-sectional in nature (Green, 1996), but later studies of recent-onset and chronic schizophrenia have since demonstrated longitudinal predictive relationships between cognitive deficits and functional outcome in schizophrenia. Examining studies with a minimum of 6 months of follow-up and that used some aspects of community functioning as an outcome variable (social or work functioning or independent living), Green and colleagues (Green, et al., 2004a; Green, Nuechterlein, Gold, Barch, Cohen, Essock, Fenton, Frese, Goldberg, Heaton, Keefe, Kern, Kraemer, Stover, Weinberger, Zalcman, & Marder, 2004b) found that 12 of 16 longitudinal studies of chronic schizophrenia found evidence for a predictive relationship between cognitive deficits and functional outcome. We have recently published strong positive predictive results from a recent-onset schizophrenia sample (Nuechterlein, Subotnik, Green, Ventura, Asarnow, Gitlin, Yee, Gretchen-Doorly, & Mintz, 2011a), indicating that three cognitive factors accounted for 52% of the variance in predicting return to work or school. Thus, the view that cognitive deficits are a rate-limiting factor in functional outcome (Green, et al., 2004a; Green & Nuechterlein, 1999) is strongly supported for recent-onset and chronic schizophrenia.

In the initial period after onset of schizophrenia, work recovery appears to be the aspect of everyday functioning that most frequently remains impaired without specialized interventions (Ventura, Subotnik, Guzik, Hellemann, Gitlin, Wood, & Nuechterlein, 2011). Thus, we are particularly in need of interventions targeting work functioning. Returning to work or school is a key part of overall recovery and also serves to restore self-esteem and/or self-efficacy, as has been often been emphasized by Bob Liberman (Liberman, 2008; Liberman, Kopelowicz, Ventura, & Gutkind, 2002). It is noteworthy that studies have found support for relationships between neurocognitive deficits and work outcome in each of the following domains: speed of processing (Dickerson, Boronow, Ringel, & Parente, 1999; Gold, Goldberg, McNary, Dixon, & Lehman, 2002; McGurk & Mueser, 2003), attention/vigilance (Addington & Addington, 2000; Nuechterlein, Subotnik, Green, Ventura, Asarnow, Gitlin, Yee, Gretchen-Doorly, & Mintz, 2011b), immediate/working memory (Gold, et al., 2002; McGurk & Mueser, 2003; Nuechterlein, et al., 2011b), verbal learning & memory (Bryson & Bell, 2003; McGurk & Mueser, 2003; Nuechterlein, et al., 2011b), visual learning & memory (Dickerson, et al., 1999; Nuechterlein, et al., 2011b), and reasoning and problem-solving (M. D. Bell & Bryson, 2001; Bryson & Bell, 2003; Dickerson, et al., 1999).

Attempts to Improve Work Outcome in Schizophrenia

Although a majority of people with schizophrenia and other severe mental disorders report a desire for paid employment (Rogers, Anthony, Toole, & Brown, 1991; Secker, Grove, & Seebohm, 2001), the rate of employment is typically 15% or below (Drake, Bond, & Becker, 2012; Lehman, 1996; Salkever, Karakus, Slade, Harding, Hough, Rosenheck, Swartz, Barrio, & Yamada, 2007). People with psychotic disorders not only have difficulty finding paid work, but maintaining employment sometimes proves quite difficult as their social deficits and psychiatric condition create challenges at the work site (Liberman, 2008). The most successful approaches to improve work outcomes for individuals with severe mental disorders involve active “hands on” skill building and community outreach approaches, as emphasized in interventions advocated by Bob Liberman.

Supported employment, particularly Individual Placement and Support (IPS), is one way to significantly increase the rate of return to competitive employment (Bond, Drake, & Becker, 2008; Drake, et al., 2012). IPS emphasizes integration of the mental health and vocational services, rapid job search, assertive outreach, client preferences, and on-going support (Becker & Drake, 2003; Bond, 2004). More than 15 controlled studies of supported employment indicate that higher rates of competitive employment, often 50–70% for part-time work, are possible for individuals with persisting severe mental illness (Bond, 2004; Bond, et al., 2008). Overall, individuals randomly assigned to supported employment are about twice as likely to be competitively employed as active control groups that receive traditional vocational rehabilitation services (Bond, 2004; Bond, et al., 2008).

The good symptomatic recovery typical of the initial period of schizophrenia (Nuechterlein, Miklowitz, Ventura, Gitlin, Stoddard, & Lukoff, 2006; Robinson, Woerner, McMeniman, Mendelowitz, & Bilder, 2004; Ventura, et al., 2011) and the relatively short interruptions in school and work history (Nuechterlein, Subotnik, Turner, Ventura, Becker, & Drake, 2008) may offer an opportunity to intervene more effectively in an attempt to prevent the development of chronic work disability. Recent applications of IPS during the initial period after a first psychotic episode suggest that the rate of returning to school or employment during this period can be as high as 80–85% (Killackey, Jackson, & McGorry, 2008; Nuechterlein, Subotnik, Ventura, Turner, Gitlin, Gretchen-Doorly, Becker, Drake, Wallace,

& Liberman, submitted; Rinaldi, Killackey, Smith, Shepherd, Singh, & Craig, 2010). This remarkable level of success of IPS in returning people with recent-onset schizophrenia to school or competitive employment does not, however, directly remediate the core cognitive deficits, which continue to predict work performance in the presence of this compensatory intervention (Nuechterlein, et al., submitted). Thus, after completing a successful randomized controlled trial of IPS in individuals with first-episode schizophrenia at UCLA, we decided that, in addition to providing IPS, we needed a direct approach to improving the core cognitive deficits in order to achieve more complete work recovery after an onset of schizophrenia.

Cognitive Remediation of Cognitive Deficits in Chronic Schizophrenia

The evidence that cognitive deficits can disrupt social and work functioning (Green, et al., 2004a; Nuechterlein, et al., 2011b) makes these deficits a very attractive target for new attempts to intervene to improve work outcome in schizophrenia (Green & Nuechterlein, 1999; McGurk & Mueser, 2004). Direct attempts to train cognitive skills are very consistent with the skills-based interventions advocated by Bob Liberman for improving social and work skills (Liberman, Mueser, & Wallace, 1986; Liberman, Wallace, Blackwell, Kopelowicz, Vaccaro, & Mintz, 1998), and were encouraged in his Clinical Research Center at UCLA.

Early attempts at cognitive remediation were exploratory, limited in duration, and focused on individualized training to improve performance on a single neurocognitive test (Benedict, Harris, Markow, McCormick, Nuechterlein, & Asarnow, 1994; R. Kern, Wallace, Hellman, Womack, & Green, 1996). The next step was the development of rehabilitation programs geared toward teaching general neuropsychological skills that were then assessed through separate cognitive testing (Spaulding, Reed, Sullivan, Richardson, & Weiler, 1999; Wykes, Reeder, Corner, Williams, & Everitt, 1999). In recent years, development of cognitive remediation in chronic schizophrenia has been guided by more explicit theoretical frameworks, and its efficacy has been evaluated through more systematic studies (Biagianti & Vinogradov, 2013; Wykes, Huddy, Cellard, McGurk, & Czobor, 2011). Strong evidence supporting the effectiveness of cognitive remediation in chronic schizophrenia is now available (Wykes, et al., 2011).

Although some earlier reviews of cognitive remediation in chronic schizophrenia reported mixed results (Pilling, Bebbington, Kuipers, Garety, Geddes, Martindale, Orbach, & Morgan, 2002; Suslow, Schonauer, & Arolt, 2001), more recent reviews and meta-analyses have been more favorable (McGurk, Twamley, Sitzer, McHugo, & Mueser, 2007; Wykes, et al., 2011). There are several reasons for this recent, more favorable outlook. Several well-designed randomized, controlled trials have shown benefits for cognitive remediation vs. control conditions in chronic schizophrenia (M. Bell, Bryson, Greig, Corcoran, & Wexler, 2001; Fisher, Holland, Merzenich, & Vinogradov, 2009; Hogarty, Flesher, Ulrich, Carter, Greenwald, Pogue-Geile, Kechavan, Cooley, DiBarry, Garrett, Parepally, & Zoretich, 2004; Medalia, Revheim, & Casey, 2000; Wykes, Reeder, Landau, Everitt, Knapp, Patel, & Romeo, 2007b), the effects appear to be reasonably durable (M. Bell, Bryson, & Wexler, 2003; Fiszdon, Bryson, Wexler, & Bell, 2004; Medalia, Revheim, & Casey, 2002; Wykes, et al., 2007b), and in some studies community functioning was also improved, particularly when cognitive remediation was part of an active rehabilitation program (M. D. Bell, Bryson, Greig, Fiszdon, & Wexler, 2005; Wykes, et al., 2011; Wykes, Reeder, Williams, Corner, Rice, & Everitt, 2003). The effect size for cognitive remediation in chronic schizophrenia was found to be 0.45 for global cognition in a recent meta-analysis of 38 studies (Wykes, et al., 2011), suggesting that perhaps one-quarter to one-third of the cognitive deficit is being reversed. Several important issues are still unresolved, including the advantages and disadvantages of so-called “bottom-up” vs. “top-down” approaches to restoring cognitive functioning, identification of the critical elements that promote transfer of effects to community functioning, and the extent to which earlier intervention with cognitive remediation might yield larger cognitive gains and broader impact on community functioning.

“Bottom-Up” versus “Top-Down” Approaches

All restorative approaches to cognitive remediation emphasize training of new skills or reactivating previously acquired cognitive skills that became dormant or inefficient. However, they differ in the extent to which they emphasize initially focusing on basic or elementary perceptual or cognitive processes versus focusing predominantly on higher-level cognitive processes. The distinction between “bottom-up” and “top-down” cognitive remediation approaches is clearly an oversimplification but it is a useful conceptual tool for discussing differences in emphasis. Saperstein and Kurtz (Saperstein & Kurtz, 2013) make a similar but not identical distinction between “drill-and-practice” and “strategy-based” approaches in their recent discussion of cognitive remediation in schizophrenia.

Bottom-up approaches typically assume that it is either necessary or efficient to start systematic cognitive training with the low-level sensory, perceptual, and cognitive processes that are deficient in schizophrenia (M. Bell, et al., 2001; M. Bell, Fiszdon, Greig, Wexler, & Bryson, 2007; Fisher, et al., 2009; Fisher, Holland, Subramaniam, & Vinogradov, 2010). These approaches, which have been strongly influenced by animal studies of neuroplasticity and human studies of rehabilitation after brain injury, typically involve extensive initial training with simple sensory discrimination and perceptual processing tasks. The level of task difficulty is gradually increased and the complexity of cognitive processes is increased, thereby building cognitive processes from “bottom-up”. Typically a large number of training trials for each elementary cognitive process are used, with gradual adjustments in difficulty level with learning to ensure that the success rate remains high. In some versions of this approach, the cognitive exercises in later stages of training directly involve higher-order cognitive processes (M. Bell, et al., 2001), while in other versions the improvements in lower-level processes are hypothesized to generate input to higher-level processes that allows improved higher-level problem-solving and strategic processes without direct training (Adcock, Dale, Fisher, Aldebot, Genevsky, Simpson, Nagarajan, & Vinogradov, 2009; Fisher, et al., 2009).

The top-down approach to cognitive remediation assumes that higher-order and more complex cognitive processes that are dysfunctional in schizophrenia can be efficiently improved through direct training at this level (Medalia, Revheim, & Herlands, 2009; Wykes

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& Reeder, 2005). This approach emphasizes training in high-level memory processes, reasoning and problem solving (Medalia, et al., 2002), other complex executive functions (Wykes, et al., 1999), and sometimes also metacognition (“thinking about thinking”) (Wykes & Reeder, 2005). Strategies for completing cognitive tasks are often explicitly trained. Some versions of the “top-down” approach also emphasize that the cognitive training exercises should involve contexts that simulate everyday life rather than only exercises that focus on specific cognitive exercises that are similar to neuropsychological test items (Medalia, et al., 2009). Often the emphasis on contexts of everyday life extends beyond the cognitive exercises themselves to use of a “bridging group” in which ways to transfer the lessons from the cognitive training sessions to everyday functioning are explicitly discussed and practiced. “Top-down” approaches vary in the degree they personalize training to also include specific training for lower-level processes, but in their purest form assume that it is possible to meaningfully modify higher-level cognitive functions in schizophrenia without intensive direct training to improve the deficits in low-level sensory and perceptual processes.

A prominent example of the bottom-up approach is Neurocognitive Enhancement Therapy (NET) (M. Bell, et al., 2001; M. Bell, et al., 2003), which involves the use of cognitive remediation programs originally developed for people with traumatic brain injury (Bracy, 1994). Elementary perceptual and simple attentional focusing skills are initially trained through repeated drill and practice exercises using computer programs from the CogRehab series developed by Psychological Software Services (Bracy, 1995). As criterion levels of performance are reached in these low-level processes, the modules from the CogRehab series then progress to working memory and long-term verbal and visual memory. Several studies by Bell and colleagues have shown that neurocognitive skills can be improved using NET in the context of a work therapy (WT) program (M. Bell, et al., 2001; Bryson & Bell, 2003). The group receiving NET+WT compared with WT alone showed significant improvement in executive functioning and working memory (M. Bell, et al., 2001). Of those participants who received NET+WT, 60% improved on some measure of neurocognition and many of those individuals showed significant improvement in executive functioning and working memory. In fact, the number of people with normal working memory performance increased significantly from 45% to 77% as compared to an overall decrease for those receiving WT alone.

After establishing the efficacy of NET for improving neuropsychological skills of people with long-term, persistent schizophrenia, subsequent studies addressed the issues of durability and generalization of the effects. Bell, Bryson, and Wexler (2003) suggested that the durability of the training effect of NET might be attributed to the length and the intensity of their drill-and-practice approach. Studies that involved follow-up of cognitive remediation training indicated that the effects of remediation can be durable and can generalize to improvement in social and work outcomes in individuals with chronic schizophrenia (M. Bell, et al., 2003; M. D. Bell, et al., 2005; Fiszdon, et al., 2004). Participants who achieved good working memory in a combined NET+WT program had more work hours and more money earned 6 months after the intervention was completed as compared to control participants with good working memory at follow-up (M. D. Bell, et al., 2005; Greig, Wexler, & Bell, 2004).

Neuropsychological Educational Approach to Remediation (NEAR) (Medalia, Revheim, & Casey, 2001; Medalia, et al., 2009) is an example of an approach that emphasizes top-down training, as it includes more direct training of complex memory strategies and problem solving than many other approaches. NEAR uses educational software programs originally developed for training cognitive skills of adolescents in educational settings. While some of the programs utilized in NEAR also involve relatively simple cognitive processes, they do not routinely isolate low-level sensory or perceptual processes for a large number of drill-and-practice trials the way that most bottom-up approaches do (Medalia, et al., 2009). A key principle for facilitating generalization and durability of gains from cognitive remediation in NEAR is incorporation of proven educational learning principles that teach fundamental problem-solving strategies, such as concept formation, reasoning, and planning (Medalia, et al., 2002; Medalia, et al., 2009). NEAR uses computer-based tasks designed to promote intrinsic rather than extrinsic motivation, based on the belief that the effectiveness of cognitive remediation depends largely on participants' perception of the tasks as inherently interesting, engaging, and relevant to real-world functioning. Intrinsic motivation, active learning, and task engagement are promoted through participant control of non-essential aspects of the learning environment, multisensory presentation of software programs, and personalizing the learning material. Versions of NEAR have been shown to improve memory as well as problem solving (Medalia, et al., 2000, 2001). Improvements in problem solving with NEAR were sustained at a 4-week follow-up point and, for a subgroup of participants, improvements in neuropsychological performance generalized to improved independent living skills (Medalia, et al., 2002).

Tailoring Cognitive Remediation for the Early Phases of Schizophrenia

If cognitive remediation interventions can be effectively adapted to be age-appropriate and engaging for individuals in early phases of schizophrenia, they might be expected to produce even larger cognitive benefits and greater transfer to everyday functioning than in people with chronic schizophrenia, given that gains would occur before personal discouragement, any further decrements in cognitive functioning, and chronic patterns of work disability have been established. It is also quite possible that neuroplasticity may be greater early in the illness, before any further brain gray and white matter loss (Andreasen, Nopoulos, Magnotta, Pierson, Ziebell, & Ho, 2011; Bartzokis, 2002; Bartzokis, Nuechterlein, Lu, Gitlin, Rogers, & Mintz, 2003).

The impact of cognitive remediation in the initial years of schizophrenia has only recently begun to be systematically studied (Fisher, Loewy, Hardy, Schlosser, & Vinogradov, 2013). Results from four studies that focused on improving core cognitive deficits in participants who were within the first eight years of schizophrenia have been published thus far.

An initial study by Ueland and Rund focused on 26 adolescents (mean age of 15 years; duration of illness unclear) who had a psychotic disorder or schizophrenia spectrum personality disorder (Ueland & Rund, 2004, 2005). Four cognitive remediation modules from Brenner and colleagues (Brenner, Hodel, Roder, & Corrigan, 1992) administered for 30 hours led to no immediate significant between-group effects but did show significant differential improvement on the span of apprehension at one-year follow-up when IQ was covaried. While between-group effects were generally not significant in this small initial study, within-group tendencies suggest that the sample size may have prevented detection of promising moderate effects on cognitive functioning.

Wykes and colleagues (Wykes, Newton, Landau, Rice, Thompson, & Frangou, 2007a) completed a randomized controlled trial of individual cognitive remediation with individuals who had an adolescent onset of schizophrenia and duration of illness less than three years. The 40 individual sessions of Cognitive Remediation Therapy (Wykes & Reeder, 2005) emphasized memory, complex planning, and problem solving using paper-and-pencil materials. This top-down training approach included explicit discussion and rehearsal of strategies for regulation, organization, and monitoring of behavior. The Cognitive Remediation Therapy group achieved a significantly higher number of categories on the Wisconsin Card Sorting Test relative to the standard care group, suggesting an impact on cognitive flexibility. No differential group effect was found for everyday functioning.

A randomized controlled trial at the University of Pittsburgh focused on people in the first eight years of schizophrenia, using a broad-based approach that included bottom-up computer programs from CogRehab (Bracy, 1995) but also weekly interactive social problem-solving group sessions (Eack, Greenwald, Hogarty, Cooley, DiBarry, Montrose, & Keshavan, 2009). This Cognitive Enhancement Therapy (CET) approach produced moderate neurocognitive gain after two years (but not one year) and resulted in significant improvements in social cognition, cognitive style, social functioning, and competitive employment (Eack, et al., 2009; Eack, Hogarty, Greenwald, Hogarty, & Keshavan, 2011). Gains in cognition from baseline to two years were significantly correlated with functional outcome gains (Eack, Pogue-Geile, Greenwald, Hogarty, & Keshavan, 2011). Gray matter volume was also better preserved over two years in the left hippocampus, parahippocampal gyrus, and fusiform gyrus in the CET group compared to the enriched supportive therapy comparison group (Eack, Hogarty, Cho, Prasad, Greenwald, Hogarty, & Keshavan, 2010). While significant neurocognitive gains were relatively slow to develop, this study showed the notable potential of cognitive remediation to produce broad gains in cognition and everyday functioning in participants who were within the first eight years of schizophrenia.

A randomized controlled trial of young individuals within the first five years of schizophrenia has very recently been published, using a focused bottom-up cognitive training approach, the Brain Fitness Program from PositScience (Fisher, Loewy, Carter, Lee, Ragland, Niendam, Schlosser, Pham, Miskovich, & Vinogradov, 2014). This study at the University of California, San Francisco, emphasized basic auditory processing and verbal learning, including aspects of verbal working memory, using principles of training-induced neuroplasticity (Vinogradov, Fisher, & de Villers-Sidani, 2012). Forty hours of training was completed on laptop computers in home settings rather than at the clinic. Compared to participants who played computer games not intended to improve cognition, participants in Brain Fitness Program training showed significant and reasonably large improvements in global cognition, verbal learning and memory, and problem solving (Fisher, et al., 2014). This amount of bottom-up cognitive training over two to three months, without a bridging group or other active rehabilitative program, did not produce functional outcome gains. It is unclear whether a longer training period or active interventions to facilitate transfer of learning would be needed to broaden the impact to everyday functioning.

In summary, studies of cognitive training for the initial years of schizophrenia have thus far used quite a range of cognitive remediation approaches, varying in bottom-up vs. top-down emphasis, targeted cognitive domains, use of paper-and-pencil vs. computerized materials, and active rehabilitative program context. The optimal approach to cognitive remediation in the initial period after onset of schizophrenia remains unclear.

Integrating Bottom-Up and Top-Down Cognitive Training for the UCLA First-Episode Study

Based on our review of the literature in 2006 during the planning of our UCLA randomized controlled trial of cognitive remediation in first-episode schizophrenia, we concluded that there were advantages and disadvantages to each of the established approaches to cognitive remediation that had been successfully applied to chronic schizophrenia. The bottom-up approaches have the advantages of isolating basic cognitive functions, even some of the simplest processes that are dysfunctional in schizophrenia, and providing repeated practice with gradually increasing difficulty level to optimize systemic gains using core principles of learning and neuroplasticity (M. Bell, et al., 2001; Bracy, 1994; Mahncke, Bronstone, & Merzenich, 2006; Vinogradov, et al., 2012). Programs using a bottom-up approach also often include detailed graphic feedback on the improvement of individual participants in separate cognitive domains, which aids evaluation of learning progress. The intensive drill-and-practice focus on lower-level processes, however, tends to make the cognitive training sessions rather repetitive and not naturally engaging. Given the typical onset of schizophrenia in late adolescence and young adulthood, a cognitive training program using solely such computer programs would appear not to be sufficiently engaging to achieve optimal treatment adherence. In addition, the bottom-up computer programs often train the basic perceptual and cognitive processes without explicit bridges to life-like contexts. Given the limitations in schizophrenia in detecting and incorporating relevant context to guide cognition (Barch & Braver, 2005; Barch, Carter, MacDonald, Braver, & Cohen, 2003; Cohen, Braver, & O'Reilly, 1996), explicit bridges to everyday life contexts would appear to be an important element of cognitive training for this disorder to facilitate transfer of learning to everyday functioning.

Top-down approaches to cognitive remediation have the advantage of placing greater emphasis on complex problem solving skills that have clearer relevance to everyday living situations (Medalia, et al., 2009; Wykes & Reeder, 2005). Typically the computer programs used in top-down approaches are more intrinsically engaging than those used in bottom-up approaches due to use of game-like formats and sophisticated graphics (Medalia, et al., 2001; Medalia, et al., 2009) (but this is now changing with new bottom-up programs from PositScience and other developers). Some top-down computer programs involve exercising complex cognitive functions in on-screen contexts that simulate real life situations (Medalia, et al., 2009). This life-like simulation seems to have promise for helping people with schizophrenia generalize their learning from the training sessions to everyday functioning. The focus of top-down approaches on complex cognitive functions, on the other hand, typically makes it very difficult to target any specific cognitive process, as higher-order cognitive processes by their nature involve the integration of several mid-level and low-level processes. Furthermore, although successfully improving complex problem solving, strategic planning, and metacognitive processes certainly would be expected to exert a top-down focusing and organizing influence on low-level sensory, perceptual, and other preattentive processing deficits in schizophrenia, it is difficult to believe that training primarily higher-order processes would fundamentally resolve deficits in low-level sensory and perceptual processing (Butler, Martinez, Foxe, Kim, Zemon, Silipo, Mahoney, Shpaner, Jalbrzikowski, & Javitt, 2007; Javitt, 2009). Thus, although it is ultimately an empirical question, emphasizing training in only higher-level cognitive processes would appear to address only part of the basic cognitive deficits in schizophrenia.

Based on this analysis of the existing cognitive remediation literature on schizophrenia, and considering our emphasis on young people with first-episode schizophrenia, we decided to combine what we viewed as the strengths of the existing approaches. Thus, for our UCLA randomized controlled trial with individuals with a first episode of psychosis in the previous two years, we used a combination of initial intensive training in visual tracking and processing speed with simple perceptual stimuli, training in attentional focusing and divided attention, and finally training in increasingly complex working memory, problem solving, and other executive processes. Within each cognitive remediation exercise, participants moved from simple to increasingly difficult levels as they met criterion levels of performance. We also established procedures to allow participants to help in the recording of their progress in the computerized training, as this aids in their sense of active participation in the process. This participant recording feature is similar to approaches developed by Bob Liberman in which participants in training workshops had workbooks that were used to record responses to the training process, lessons learned, and strategies that could be used to improve community functioning.

We formed a collaboration among researchers in our UCLA first-episode schizophrenia group and cognitive remediation leaders at Yale (Morris Bell) and Columbia (Alice Medalia) to guide the selection of software for our project. We drew almost all of the computer programs for lower-level cognitive processes from the PSS CogRehab software (Bracy, 1995) that had been successfully applied with people with chronic schizophrenia within NET (M. Bell, et al., 2001; M. D. Bell, et al., 2005). The PSS CogRehab programs use a highly structured “bottom-up” approach that allows each participant to move through a series of cognitive tasks ranging from visual tracking speed to attentional control and response inhibition and finally to verbal and visual memory. We combined the drill-and-practice CogRehab exercises with a few game-like exercises of simple cognitive functions from NEAR (Medalia, et al., 2009) in order to enhance engagement in the initial training sessions. In contrast, as we moved from lower-level and mid-level cognitive processes to high-level ones, we drew mainly from the educational software characterizing NEAR (Medalia, et al., 2009). The NEAR software involves engaging graphics and auditory feedback and in some instances also simulations of real-life social or work situations.

We also adopted from NET and NEAR the use of a cognitive trainer in a small-group computerized lab setting to guide the participants through the phases of the program. The

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cognitive remediation trainer tracked each individual's progress and offered support, guidance, suggestions, and praise for progress on the cognitive exercises.

Cognitive Remediation Sessions in the UCLA First-Episode Schizophrenia Study

Cognitive Training Exercises—Participants in the Cognitive Remediation condition participated in a computer-assisted cognitive training program for six months, two hours per week, followed by only one hour per week of computerized training for another six months. A series of 23 cognitive training exercises were used, each of which involved a computer-based task with graduated levels of difficulty. The cognitive training targeted processing speed, attention, working memory, verbal and visual learning and memory, and problem solving, cognitive domains that are deficient in schizophrenia and are predictive of functional outcome (Green, et al., 2000; Nuechterlein, et al., 2004). The collaborative team selected a set of cognitive training exercises that 1) had been demonstrated to lead to cognitive improvement in people with chronic schizophrenia, 2) provided excellent balance between sufficient training in basic cognitive domains and training in more complex reasoning and problem solving skills, 3) provided ongoing feedback on performance such that people are immediately reinforced for correct responses, 4) allowed progression from simple to more difficult examples within each computer program to keep the number of errors during training low, and 5) were appropriate for individuals with a recent onset of schizophrenia. The specific computer programs used to train the increasing complex cognitive processes are listed in Table 1.

Participants moved through three successive phases of computer-assisted cognitive training. The initial phase, Foundations, emphasized basic visual tracking speed, focused and divided attention, and working memory skills. It included substantial practice with tracking tasks to shape processing speed and sequential recall tasks to improve working memory. The second phase, Intermediate Skills, emphasized verbal learning and memory (beyond capacity limits of working memory), verbal categorizing, recall of paired associates, and simple levels of reasoning and problem solving. The third phase, Complex Skills, involved a series of high-level reasoning and problem solving exercises that continue to use lower-level cognitive skills, but emphasize training in the use of cognitive strategies and other executive skills to achieve specific goals. In the last group of computer programs, the cognitive skills are exercised in situations with increased contextual relevance for everyday life, including simulations of work situations that require planning and decision-making.

Participants completed their computerized cognitive training in one-hour group cognitive remediation sessions (4–5 participants in a group). Trained staff research associates assisted in cognitive remediation training, maintain approximately a 4:1 ratio of participants to staff. The cognitive remediation trainers provided each participant with the sequence of programs to be used in a session, helped participants start each program initially, monitored individual progress on the programs to enhance learning and avoid frustration, and helped to record skill acquisition progress. The cognitive remediation sessions occurred at the Aftercare Research Program on the UCLA campus.

Participants moved from simple to more difficult levels within each computer program when they achieved an operationally defined criterion of success. The cognitive training sessions were arranged so that amount of exposure to each program during the required activity time (45 minutes per session) was equivalent across participants. In addition, to enhance the participant's sense of choice in this learning experience and to maximize task engagement, each patient was allowed to choose which the computer program to use during the last 15 minutes of each session. All of the programs with which the participant had gained experience at that point during cognitive remediation were available for this elective activity time. In addition to the intrinsically rewarding quality of the experience with several of the programs chosen for this cognitive remediation program, engagement in cognitive remediation was rewarded by providing $20 for every 10 hours of participation in cognitive remediation sessions.

Bridging Group—The procedures we used in the Bridging Group are perhaps the best direct example of the embodiment of Bob Liberman's vision of encouraging people to be active participants in their treatment. The cognitive coaches used manualized approaches to the delivery of a behaviorally oriented, hierarchal approach to building bridges from the skills developed in the cognitive training computer programs to community functioning. We used techniques such as goal setting, role playing, and suggestions from fellow participants and staff during practice of practical skills in the supportive group environment. We reviewed written materials in the bridging group sessions, and encouraged participants to review those written tools again with their case managers and family members outside of the group setting.

As developed within both NET (M. Bell, et al., 2001) and NEAR (Medalia, et al., 2009), in our UCLA randomized controlled trial of cognitive remediation with individuals with a recent first episode of schizophrenia, we included a weekly Bridging Group throughout the 12 months of cognitive remediation. The Bridging Group was designed to facilitate connections between the computer-assisted cognitive remediation and work/school performance and to aid in setting and tracking individualized work/school goals for each participant. Participants attended this ½-hour group led by the IPS specialist and a cognitive remediation trainer. Thus, the total cognitive remediation time was 2.5 hours/week for the first six months. The cognitive trainer and the IPS specialist helped to bridge learning from the cognitive training sessions to work/school situations through discussion of specific examples raised by the individual participants. Progress in the computer-assisted cognitive remediation sessions was also discussed, with participants with more cognitive training experience being encouraged to support and suggest strategies to those in earlier stages of training. The participants took turns in successive weeks reporting and discussing whether or not they achieved their individual goals and setting new goals, as appropriate.

Discussion

This article describes the scientific background and theoretical approach that we used to develop a cognitive remediation intervention adapted to the initial period after a first psychotic episode. The cognitive remediation approach that we adopted for our UCLA randomized controlled trial reflected our evaluation of the advantages and disadvantages of existing bottom-up and top-down cognitive training approaches. We integrated computerized cognitive training programs drawn from both a predominantly bottom-up model (NET) (M. Bell, et al., 2001; M. D. Bell, et al., 2005) with those from a predominantly top-down model (NEAR) (Medalia, et al., 2009) to create an approach that trained lower-level perceptual speed and attentional abilities, mid-level memory skills, and high-level reasoning and problem solving abilities. We also included a weekly group session that explicitly bridged between the lab-based computer sessions and actual situations from the daily work and school lives of the participants. Finally, we worked to balance the desire for sufficient practice with each cognitive process with the need to continue to actively engage the participants and facilitate the transfer of learning to everyday life.

Our approach to cognitive remediation was clearly influenced by the core features that Bob Liberman emphasized for interventions throughout his distinguished career in psychiatric rehabilitation (Liberman, 1992, 2008). Our approach is skills oriented and employs a hierarchical teaching strategy. It is broadly behaviorally oriented, including components of goal setting, coaching, and role playing that are similar to those in social skills training. Finally, we include a focus on community applications of the skills learned, with an overall goal of maximizing recovery of work and social functioning.

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Table 1

Cognitive Training Programs: Listing of Target Skills and Cognitive Exercises

Target Skills	Name of Cognitive Exercise	Brief Description
Phase I – Foundations		
Processing speed and sustained attention	Visual Tracking I	Tracking a line moving at an increasingly rapid pace and responding to occasional color changes
Processing speed, attention, and inhibition	Simple Choice Visual Reaction	Responding as quickly as possible to colored target appearance and inhibiting responses to stimulus of different color
Processing speed and attention to multiple dimensions	Simultaneous Multiple Attention	Tracking up to four lines moving at an increasingly rapid pace and responding to occasional targets in each
Processing speed, attention to multiple objects, and inhibition	Frogger	Moving a frog along a path and avoiding oncoming objects, with increasing difficulty due to increasing speed and number of objects
Working memory – verbal	Sequenced Recall Digits Visual	Immediate memory for visually presented digit sequence, forward and reversed
Working memory – verbal	Sequenced Recall Words Visual	Immediate memory for sequence of visually presented words, with number of words increasing over trials
Working Memory – spatial	Spatial Memory	In a sequence of rooms on computer screen, need to choose correct door to enter the next room, with each entered room looking identical
Immediate spatial and object memory	Frippeltration	Immediate memory for objects, colors, or sound associated with a position in a grid, to allow matching the squares with identical features
Phase II – Intermediate Skills		
Object memory – intermediate level	Recognition Recall	Recognition of pictures of objects after a 5–180 second delay, selecting from a larger array of displayed and non-displayed objects
Verbal memory and categorization – intermediate level	Verbal Memory Categorizing	Verbal memory after 1–60 second delay of words and their semantic categorization
Visual-verbal associative memory – intermediate level	Paired Associates Recall	Memory for pairings of graphics designs and numbers after delays of 1–60 seconds
Verbal learning and memory – intermediate level	The Phone Message	Memory for information presented within a simulated phone message, with questions in a multiple-choice format
Problem Solving – simple visual categorization and reasoning	Frippel Place	Placement of cartoon characters in a simulated apartment house based on their physical characteristics
Problem Solving – simple component analysis, pattern recognition, and reasoning	Factory	Placement of machines on an assembly line in the correct order to create geometric products, using visual reasoning and problem-solving skills to analyze component processes, recognize patterns and sequences, and predict outcomes
Problem Solving – simple reasoning to achieve a specific goal	Stocktopus	In a simulated stock exchange work setting, participant makes a series of trades of objects to acquire the goal objects
Problem Solving – simple visual sequential reasoning	Pyramids	Starting with a pyramid formed of different sizes of disks on a post, participant moves the disks, one at a time, so that they end up as a correct pyramid on another post
Phase III – Complex Skills		
Complex problem solving in a game-like setting	Carmen Sandiego	Participant is detective who must gather clues by asking questions of witnesses and travelling to different locations in order to solve thefts

Target Skills	Name of Cognitive Exercise	Brief Description
Complex reasoning and problem solving in a simulated work setting	Math for the Real World	Simulation in which participant is a roadie with a hot new rock band, faced with varying situations in which negotiations for cash are needed to shoot a video to promote the band
Complex reasoning and problem solving in a simulated work setting	Grammar for the Real World	Contextualized as a TV studio in which the participant is an intern who must take on editing and writing assignments for different show business professionals
Complex reasoning and problem solving in a simulated work setting	Ice Cream Truck	Simulated business of managing an ice cream truck, with required complex decisions involving selecting a product mix, setting prices, and arranging advertising
Complex reasoning and problem solving involving multilevel strategy situations	Mission Think	Participant solve five different strategy games that are multi-level and have no time limits, using a range of verbal and visual information
Complex reasoning and problem solving using hypothesis testing and error correction skills	Mountain Rescue	A simulated mountain rescuer uses logical thinking skills involving comparing, sorting, graphing, testing hypotheses, sequencing, mapping, testing cause and effect, spatial reasoning, predicting, following directions, and organizing data
Complex reasoning and problem solving involving logical and creative thinking in adventurous game-like setting	Logic Quest	A simulated adventure in which participant helps captives make their escape from enemies using combinations of features of captives to overcome obstacles using deductive logic and creative reasoning