Cognitive Remediation for Schizophrenia:

An Expert Working Group White Paper on Core Techniques

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Abstract:

Cognitive remediation is now widely recognized as an effective treatment for cognitive deficits in schizophrenia. Its effects are meaningful, durable, and related to improvements in everyday functional outcomes. As with many therapies, the evolution of cognitive remediation has resulted in treatment programs that use a variety of specific techniques, yet share common core principles. This paper is the product of a cognitive remediation expert working group consensus meeting to identify core features of the treatment and produce recommendations for its design, conduct, reporting, and implementation. Four techniques were identified as core features of cognitive remediation: facilitation by a therapist, cognitive exercise, procedures to develop problem-solving strategies, and procedures to facilitate transfer to real world functioning. Treatment techniques within each of these core features are presented to facilitate decisions for clinical trials and implementation in clinical settings.

Cognition has become a clear target for intervention given its relationship to outcomes and recovery in many different disorders. This pervasive relationship of cognition to outcome is most noticeable in schizophrenia where it appears prior to the disorder, is related to outcomes and also limits recovery even when other support has been provided. A therapy called cognitive remediation evolved to improve recovery in this disorder but recently there has been some debate about the key ingredients. It is essential to move the field to the point where these cognitive remediation therapies can be rolled out into mental health services, but first we need a clear understanding of the core techniques comprised in the therapy. Recently, we saw the publication of the eCaesar study (Mahncke et al., 2019), which showed no benefits. The authors of this paper, leaders in the field of cognitive remediation, believe that several of the key cognitive remediation ingredients were not provided in the active therapy condition and so the study should not be considered an adequate cognitive remediation trial. To aid the research field as well as clinicians implementing therapy, this paper sets out what would be considered acceptable ingredients as well as pointing out areas that need further investigation.

Cognitive remediation has emerged as an evidence-based treatment for cognitive impairments in schizophrenia. Defined by the Cognitive Remediation Expert Working group: "Cognitive remediation is a behavioral training intervention targeting cognitive deficit (attention, memory, executive function, social cognition, or metacognition), using scientific principles of learning, with the ultimate goal of improving functional outcomes. Its effectiveness is enhanced when provided in a context (formal or informal) that provides support and opportunity for extending to everyday functioning" (Cognitive Remediation Experts Working Group, 2010). The treatment is unique among our behavioral and pharmacological therapeutic arsenal in treating one of schizophrenia's core features - cognitive dysfunction. Meaningful and sustained

improvements in cognitive abilities are observed in most (Bell et al., 2003; Bowie et al., 2012; Fiszdon et al., 2004; McGurk et al., 2005; Penadés et al., 2006; Wykes et al. 2003), but not all (Dickinson et al., 2009) randomized controlled trials. Enhanced everyday functioning and reduction of disability are also goals of cognitive remediation, given the robust and stable relationship of cognitive functions to everyday functioning. However, compared to commonly reported gains in cognition, improved community functioning following cognitive remediation has been more variable across studies in schizophrenia. Meta-analytic findings suggest that functional improvements from cognitive remediation are moderated by whether participants are also engaged in additional rehabilitation programs such as those that focus on work, independent living, or adaptive living skills and also whether the remediation approach has a strong strategic learning component (Wykes et al. 2011).

In the context of strong empirical evidence that cognition can be improved, there is a need for more clarity about the key elements of the treatment. Research and clinical initiatives would benefit from a consensus on the components that are central to any treatment fidelity assessment, will guide reviews of existing and future studies, and clarify decisions of which components are brought to real world placements. To this end, the authors of this paper met as a working group of experts in the design and implementation of cognitive remediation programs with the goal of providing a consensus statement on the core features of cognitive remediation. We provide more granular guidance on components of cognitive programs, including issues related to the core aspects of cognitive exercise and how the cognitive remediation therapist can stimulate improved use of problem solving strategies and increase the likelihood of transferring skills developed in treatment to everyday functioning goals. The working group recognizes that some procedures will continue to vary – the intention of this paper is not to mandate components

of treatment, but to provide a clearer way for studies to report how their treatment was implemented and for clinicians to use this framework to make treatment implementation decisions when using cognitive remediation.

Components of Cognitive Remediation Programs

The working group process included a half-day in-person meeting to identify core features of cognitive remediation, followed by contributions by all authors to the value of each of the procedures in boldface below and revisions to the manuscript. The working group identified four components of cognitive remediation: a trained therapist, the practice of cognitive exercises, attention to the development of cognitive strategies, and procedures to facilitate transfer of cognitive gains to everyday functioning. These four procedures are those that are used in many, but not all programs. The specific content and proportion of time devoted to each procedure varies across existing programs.

1. *Cognitive Remediation Therapists:*

Although computerized cognitive training is a core feature of cognitive remediation programs, computer cognitive training *alone* is *not* considered cognitive remediation in the absence of a trained therapist (Harvey et al., 2018). Cognitive remediation studies have reported a wide range of therapist characteristics. In some programs, the therapist takes a more active role in facilitating discussions, addressing negative beliefs about the participant's cognitive or functional abilities, and promoting activities within and outside of sessions to motivate behavior change in daily life. **Reports of cognitive remediation should specify the background**

training of therapists. The working group agreed that **the therapist should have a basic understanding of cognitive processes, how cognitive deficits manifest in mental disorders, and how these cognitive abilities affect everyday functioning.** While there is a preference for scholarly work and supervised practice in this area, the working group recognized that not all sites are equipped with clinicians who have this degree of training. In this case, the therapist should undertake a structured training program or mentorship to acquire this knowledge and skills. Examples can be found in existing programs that provide training and certification.

Many participants enter cognitive remediation without a clear language of cognitive functions and without a clear set of short- and long-term goals for functioning. **It is helpful for the therapist and the participant to formulate the cognitive problem and link this problem to goals.** An assessment of cognitive functioning prior to treatment can be used to demonstrate a profile of strengths and weaknesses, allowing the therapist to discuss how most people have variability in their cognitive abilities. The therapist should work collaboratively with the participant to identify cognitive skills that are a priority for the participant, recognizing that the participants' subjective views of their abilities might not align with objective measures. The therapist should work collaboratively with the participant to identify everyday functioning goals that can be linked to the cognitive remediation treatment environment (for example, the training, strategies, transfer techniques discussed below). **Therapists in cognitive remediation work with participants to track progress toward goals, identify barriers, and adjust short- and long-term goals as needed.**

2. *Cognitive Exercise:*

A core feature of cognitive remediation programs is cognitive exercise aimed to improve cognitive functioning. Enhancement of cognitive abilities is typically addressed with computer-based drill and practice techniques, in which the participant engages repetitively with stimuli that are associated with targeted cognitive domains and produce activation of neural networks associated with those cognitive deficits. **The expert working group agreed that it is important for participants to engage in multiple repetitions of an exercise** to sustain activation of the associated neural networks, provide a sense of mastery, and allow for the practice of multiple strategies. The precise number of repetitions for any one exercise to exert effects is not yet known and is an area in need of further study. **The working group agreed that intensive training is ideal to produce meaningful effects.** Although there are no published comparative 'dosing' studies of cognitive remediation, effective programs have provided two to three sessions per week; the minimum time for training tends to be 20 hours, though 40 or more hours of training is common. One meta-analysis found the average length of treatment was 32.2 hours (range=4–130), provided across 16.7 weeks (range=2–104) (Wykes et al., 2011). **Cognitive remediation treatment includes a plan for orienting participants to the program, including how to navigate a computer program and how to engage with non-computerized tasks.** This might take the form of an explanation or demonstration delivered clearly by a therapist. The working group recommends the involvement of a therapist as opposed to a self-learning or purely computer-driven orientation, to ensure an adequate understanding of the purpose and mechanics of the program through the opportunity for discussion and demonstration. **Each cognitive exercise should be explained to the participant prior to training.** This might take the form of a therapist explaining and/or demonstrating the task. When task instructions are provided by a computer program, a facilitator or therapist should be available to expand on the

information if necessary. **Supplementation of in-session training with homework activities is sometimes used.** Homework might include continued drill and practice sessions, engaging in daily activities associated with the cognitive strategies developed in sessions, and applying cognitive strategies to aid acquisition of functioning goals.

The cognitive training stimuli are most often delivered by a computerized program, and many of these programs offer the ability to titrate task difficulty to match the individual participant's response levels. For example, after completing several trials in an exercise and achieving several consecutive scores of over a certain threshold (e.g., 80% accuracy), the exercise might change by adding more stimuli to encode, introduce distracting information, reduce encoding or response time, or minimize the distinguishing features of training stimuli such as those that are targets or distractors. Conversely, performance below a certain threshold (e.g., 70% accuracy) might prompt the program to reduce the difficulty by adjusting these parameters. This process continuously adjusts to keep the participant in a training zone that remains challenging but not beyond current abilities that would limit the chance for success -- building on the tenets of neuroplasticity, that learning is novel, challenging, and rewarding. Other cognitive remediation programs do not use the adaptive feature of computer software in favor of evaluation of actual performance scores, including performance changes based on task complexity. These approaches instead use a standardized curriculum that slowly increases exercise complexity, independent of participant response levels. These programs use facilitation to teach participants the skills and abilities to meet the increasing challenge and to optimize learning from any errors participants make (McGurk et al., 2015). This approach increases the challenge of the exercise regardless of performance in order to maximize the use of strategy coaching. Currently, there are few studies that have examined the benefits and challenges

associated with the timing and precise decision-making algorithms that would optimize cognitive training, however, members of the **expert working group endorsed the importance of increasing the difficulty level of the cognitive exercises to keep the tasks challenging and engaging.**

Most cognitive remediation programs also include performance feedback during sessions, allowing for the participant to evaluate the effectiveness of strategies and track progress. **The working group agreed that performance parameters (e.g., accuracy, speed) should be tracked.** Program participants may write down performance scores following each exercise (McGurk et al., 2005; McGurk et al., 2015), or the computer program may track and display progress on the exercises. It is also important **that feedback be provided to the participant during the training session.** Feedback may be presented on a trial-by-trial basis or after a fixed number of trials within an exercise, to match the structure of the computerized exercise.

Feedback and praise for performance success is often provided by a therapist in addition to the visual display by the computer program. Therapist praise might take the form of highlighting progress through difficulty levels, reinforcing the development and flexible use of problem-solving strategies, or encouragement for staying focused on training even when performance has plateaued. **The working group agreed that clinician praise should weigh more heavily on the process of training (e.g., staying engaged with the task, attempting new strategies), rather than on performance.** The purpose of this focus is to capitalize on intrinsic motivation to remain engaged with the task and to avoid negative attributions associated with perceived or actual low performance. This latter issue might be particularly important given the different pace of training that participants are likely to have in a group format.

3. *Procedures to Develop Problem-Solving Strategies:*

In addition to therapist facilitation and training to enhance cognitive performance, a goal of cognitive remediation programs includes procedures to facilitate enhanced use of problem-solving or cognitive strategies. People with schizophrenia often are not aware that they use specific strategies during cognitive tasks and that at times these strategies are inefficient (Elahipanah et al., 2011; Cella et al., 2015). The range of strategies is often truncated and cognitive rigidity associated with the disorder makes it challenging to flexibly modify strategies as task parameters change or to switch strategies across tasks. **Cognitive remediation treatment includes opportunities for participants to identify and monitor strategies they use during cognitive training tasks.** Development of these 'meta-cognitive skills' is considered a critical part of cognitive remediation. Participants should have a forum for identifying and documenting their strategies and tracking success associated with each cognitive task. Group treatment opens the possibility for sharing strategies. Documentation of strategies found effective for a cognitive training task allows for a clearer link between the cognitive training task and opportunities to transfer gains to the real world. Although more data are needed to determine optimal methods for eliciting and modifying strategies, early work in healthy samples has demonstrated more success when participants use self-generated strategies (Dunning and Holmes, 2014). Still, many people with schizophrenia are likely to have a difficult time self-generating strategies, at least in the early stages of treatment. It is thus recommended that **clinicians be prepared to suggest potential strategies**, if participants struggle to produce a meaningful or a broad range of strategies.

4. *Procedures to Facilitate Transfer to Real World Functioning*

As highlighted in the prior proceedings of an expert panel (McGurk et al, 2013), and based on meta-analytic findings, in order for cognitive programs to achieve functioning improvements, psychosocial rehabilitation consonant with participants' community goals is a necessary component. **Clinicians should work with individual participants to set cognitive goals collaboratively** that have clear links to community functioning, and have multiple short-term objectives that are achievable and measurable during treatment. One strategy is to make a clear and direct link between individual goals and the participant's cognitive profile. Improvements in areas of impairment and making use of cognitive strengths can be linked to discrete objectives (e.g., improving attention could improve understanding of others during conversations; see Bowie and Gupta (2016) for further reading). Cognitive remediation provides a structured learning curriculum for developing skills that are underutilized in daily living, and to practice skills at a level of challenge beyond what might be experienced/available in the participant's natural environment. To that end, **clinicians should promote realistic expectations for the process of functional change**. For example, the procedures offered in the cognitive remediation program might consider whether the nature of the treatment goals are restorative (recovery of cognitive functions that increase success on routine tasks), rehabilitative (regaining functional skills that have been lost) or habilitative (training of new functional skills that might not have been acquired).

The process by which transfer has been facilitated varies in the literature. In some cases, cognitive remediation is embedded within a broader psychosocial rehabilitation program (McGurk at al., 2015). Group or individual discussions might be used during cognitive remediation sessions to generate specific activities that participants can link to the training activities with the goal of applying their cognitive skills in daily life (Medalia et al., 2018). Some

participants might experience challenges when relying only on discussion of real world applications, as lack of experience can inhibit skill use (Holshausen et al., 2014). A staged approach can help overcome this challenge. For example, adaptations to the cognitive exercises, such as using ecologically valid tasks (Reeder et al., 2016) or using role-plays that simulate real world environments can also provide tangible examples or direct real life practice using the strategies learned in cognitive remediation (Bowie et al., 2017). Meta-analytic and clinical trial findings suggest that transfer of cognitive gains to functioning with cognitive remediation is more likely when participants are enrolled in supplemental activities that require cognitive activation, such as vocational rehabilitation or skills training (Bell et al., 2007; Bowie et al., 2012; Eack et al, 2011; McGurk et al., 2005; McGurk et al., 2015; Wykes et al., 2011). I**t is recommended that clinicians support participation in real world transfer activities** that can be linked with the themes, cognitive skills, and strategies addressed in treatment. In planning and reporting results of cognitive remediation methods, **the techniques for transfer (e.g., discussion, role-plays, social cognition training, supplemental activities, additional psychosocial intervention) should be clearly described.** Several manuals and readings are available with explicit procedures (Medalia and Bowie, 2016; Medalia et al., 2018; McGurk and Mueser, in press; Reeder et al., 2017; Twamley et al., 2019).

Summary

Cognitive remediation for schizophrenia and other severe mental illnesses have evolved considerably over the last few decades. While there continue to be some differences across programs, this working group identified core elements that unite them under the description of cognitive remediation. These core elements include facilitation by a therapist, practicing

cognitive exercises, facilitation of cognitive and problem solving strategies, and including techniques or activities that promote the transfer of cognitive skills to real life functioning. We believe that these core elements should be considered when developing, implementing, and reporting cognitive remediation. Future work in the field will continue to inform best practices, such as therapist to patient ratio, optimal group composition, qualification and training needs for therapists, duration and schedule of treatment, and comparative effectiveness of diverse training and transfer activities described in this paper to inform what works best, and for whom.

References

Bell, M., Bryson, G., Wexler, B.E., 2003. Cognitive remediation of working memory deficits: durability of training effects in severely impaired and less severely impaired schizophrenia. Acta Psychiatr. Scand. 108 (2) 101-109.

Bell, M., Fiszdon, J., Greig, T., Wexler, B., Bryson, G., 2007. Neurocognitive enhancement therapy with work therapy in schizophrenia: a six month follow-up of neuropsychological performance. J. Rehabil. Res. Dev. 44 (5) 761-70.

Bowie, C.R., Grossman, M., Gupta, M., Holshausen, K., Best, M.W., 2017. Action-based cognitive remediation for individuals with serious mental illnesses: Effects of real-world simulations and goal setting on functional and vocational outcomes. Psychiatr. Rehabil. J. 40 (1) 53.

Bowie, C.R. & Gupta M., 2016. Addressing cognitive distortions, dysfunctional attitudes, and low engagement in cognitive remediation, in: Medalia, A., Bowie, C.R. (Eds.), Cognitive Remediation to Improve Functional Outcomes. Oxford University Press., New York, pp. 138-154.

Bowie, C.R., McGurk, S.R., Mausbach, B., Patterson, T.L., Harvey, P.D., 2012. Combined cognitive remediation and functional skills training for schizophrenia: effects on cognition, functional competence, and real-world behavior. Am. J. Psychiatry. 169 (7) 710-718.

Cella, M., Reeder, C., Wykes, T., 2015. Lessons learnt? The importance of metacognition and its implications for Cognitive Remediation in schizophrenia. Front. Psychol. 6 1259.

Cognitive Remediation Experts Working Group (CREW), Florence, April 2010.

Dickinson, D., Tenhula, W., Morris, S., et al., 2009. A randomized, controlled trial of computer-assisted cognitive remediation for schizophrenia. Am. J. Psychiatry. 167 (2) 170-180.

Dunning, D.L., Holmes, J., 2014. Does working memory training promote the use of strategies on untrained working memory tasks?. Mem. Cogn. 42 (6) 854-62.

Eack, S.M., Pogue-Geile, M.F., Greenwald, D.P., Hogarty, S.S., Keshavan, M.S. 2011. Mechanisms of functional improvement in a 2-year trial of cognitive enhancement therapy for early schizophrenia. Psychological Medicine. 41(6):1253-61.

Elahipanah, A., Christensen, B.K., Reingold, E.M., 2011. What can eye movements tell us about Symbol Digit substitution by patients with schizophrenia?. Schizophr. Res. 127 (1-3) 137-143.

Fiszdon, J.M., Bryson, G.J., Wexler, B.E., Bell, M.D., 2004. Durability of cognitive remediation training in schizophrenia: performance on two memory tasks at 6-month and 12-month follow-up. Psychiatry Res. 125 (1) 1-7.

Harvey, P.D., McGurk, S.R., Mahncke, H., Wykes, T., 2018. Controversies in computerized cognitive training. Biol. Psychiatry Cogn. Neurosci. Neuroimaging. 3 (11) 907-915.

Holshausen, K., Bowie, C.R., Mausbach, B.T., Patterson, T.L., Harvey, P.D., 2014. Neurocognition, functional capacity, and functional outcomes: the cost of inexperience. Schizophr. Res. 152 (2-3) 430-434.

Mahncke, H. W., Kim, S. J., Rose, A., et al., 2019. Evaluation of a plasticity-based cognitive training program in schizophrenia: Results from the eCaesar trial. Schizophr. Res. 208 182-189.

McGurk, S.R., Mueser, K.T., Pascaris, A., 2005. Cognitive training and supported employment for persons with severe mental illness: one year results from a randomized controlled trial. Schizophr. Bull., 31 (4) 898-909.

McGurk, S.R., Mueser, K.T., Xie, H., et al., 2015. Cognitive enhancement treatment for people with mental illness who do not respond to supported employment: a randomized controlled trial. Am. J. Psychiatry. 172 (9) 852-61.

McGurk, S.R. and Mueser, K.T. Thinking Skills for Work Program: Cognitive Enhancement for Successful Employment. Guilford Press, in press.

McGurk, S.R., Mueser, K.T., Covell, N.H., Ciccerone, K.D., Drake, R.E., Silverstein, S.M., Medalia, A., Myers, R., Bellack, A.S., Bell, M.D., and Essock, S.M. Mental Health System Funding of Cognitive Enhancement Interventions for Schizophrenia: Summary and Update of the New York Office of Mental Health Expert Panel and Stakeholder Meeting. *Psychiatric Rehabilitation Journal,* 36(3):133-45, 2013. doi: 10.1037/prj0000020.

Medalia, A., Bowie, C.R. (Eds.), 2016. Cognitive Remediation to Improve Functional Outcomes, Oxford University Press, New York.

Medalia, A., Herlands, T., Saperstein, A., Revheim, N., 2018. Cognitive Remediation for Psychological Disorders. Oxford University Press., pp. 141-168.

Penadés, R., Catalán, R., Salamero, M., et al., 2006. Cognitive remediation therapy for outpatients with chronic schizophrenia: a controlled and randomized study. Schizophr. Res. 87 (1) 323-331.

Reeder, C., Huddy, V., Cella, M., et al., 2017. A new generation computerised metacognitive cognitive remediation programme for schizophrenia (CIRCuiTS): a randomised controlled trial. Psychol. Med. 47 (15) 2720-30.

Reeder, C., Pile, V., Crawford, P., et al., 2016. The feasibility and acceptability to service users of CIRCuiTS, a computerized cognitive remediation – a training for schizophrenia. Behav. Cogn. Psychother. 44 (3) 288-305.

Twamley, E.W., Thomas, K.R., Burton, C.Z., et al., 2019. Compensatory cognitive training for people with severe mental illnesses in supported employment: a randomized controlled trial. Schizophr. Res. 203 41-48. http://www.cogsmart.com/

Wykes, T., Reeder, C., Williams, C., Corner, J., Rice, C., Everitt, B., 2003. Are the effects of cognitive remediation therapy (CRT) durable? Results from an exploratory trial in schizophrenia. Schizophr. Res. 61 (2) 163-174.

Wykes, T., Huddy, V., Cellard, C., McGurk, S.R., Czobor, P., 2011. A meta-analysis of cognitive remediation for schizophrenia: methodology and effect sizes. Am. J. Psychiatry. 168 (5) 472-485.

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***Conflict of Interest**

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