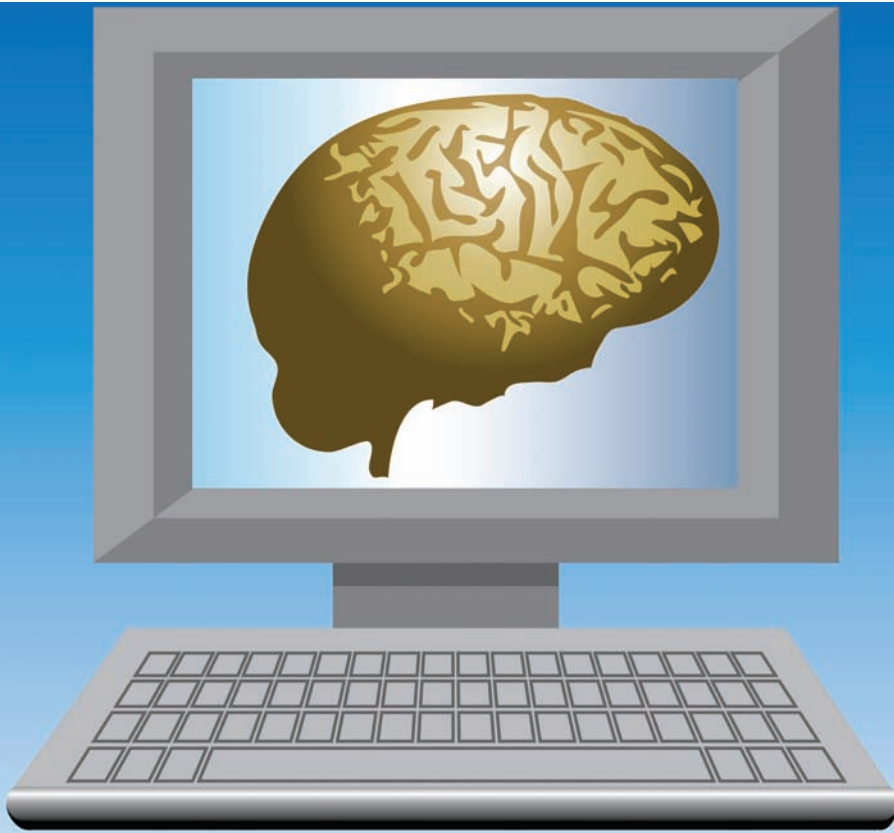


Update on Cognition



Cognitive Remediation in Severe Mental Illness

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ABSTRACT

Cognitive enhancement has received substantial recent attention because of multiple recent successes. We review the current research literature on cognitive enhancement, focusing on new developments that separate previous less successful efforts from recent successes. These innovations include increased

understanding of the dosing and spacing of sessions, the need for titration of difficulty of individual sessions, and the importance of concurrent interventions. We also review the domains of functioning shown to be improved by cognitive remediation and the possibility that some biomarkers improve as well. We close by noting that current societal

factors may impose limitations on the benefits accrued from cognitive remediation and also note that some pharmacological treatments, such as anticholinergic medications, may reduce or eliminate the potential benefits from cognitive remediation.

KEY WORDS

Cognitive remediation, disability, cognition, schizophrenia

INTRODUCTION

Cognitive remediation has recently attracted considerably more attention than during its first few decades of development. This increased attention is likely associated with a series of studies using cognitive remediation that have led to considerable success. Successes include improvements in targeted cognitive processes as well as functionally relevant changes in everyday behaviors. In addition, several of these studies have also found that biologically relevant parameters also improve with treatment and that pharmacological compounds that interfere with cognitive functioning in general also interfere with skills acquisition in cognitive remediation interventions. In this column, we describe the reasons why we believe that current interventions work where others have failed and how remaining barriers to progress could be addressed.

CURRENT INTERVENTION STRATEGIES

There are two general classes of cognitive remediation interventions delivered at present. These include bottom-up training that aims to improve basic sensory processes and top-down training focusing on higher level cognitive skills, such as attentional control. Some studies have used mixed approaches. Other attempts to improve functioning take compensatory approaches to adapt the

environment to the individual's cognitive limitations; these are theoretically different approaches that will not be reviewed here. All of the effective strategies share several features that are important.

Dynamic titration of difficulty.

Task demands and requirements respond to the level of performance on the part of patients. On good days, the task becomes more difficult and when the patient performs more poorly, the task becomes easier. Thus, progress is made because the performance of the participant is never perfect, and, hence, not cognitively challenging and never extremely poor, which would be discouraging and counterproductive. Evidence of neuroimaging studies has suggested that there are optimal levels of task difficulty that lead to maximal and appropriately localized brain activation. Computer-based drill and practice exercises often have multiple parameters that can be adjusted to find the optimal level. For example, stimuli can be presented at variable speeds, with or without distracting stimuli, and with differing number of stimuli to attend to and/or recall.

Dosing considerations. Spaced practice has been known for half a century to lead to better learning outcomes than massed practice. Just how spaced is an empirical question, but it seems likely that every day is excessive for certain skills and once a week is not enough. Many interventions deliver two 30- to 60-minute training sessions per week.¹ Greater successful completion of intervention sessions leads to better improvements. There is a clear dose-response, although the dose can be quite low in some cases (18–20 sessions)² and is likely to vary as a function of the individual's strengths and the cognitive skill being targeted.

Strategic monitoring.

Improvement in a broader range of cognitive abilities and the everyday

behaviors related to those abilities might be more likely if individuals develop flexible approaches to solving tasks. With strategic monitoring, patients are encouraged to explicate their thinking strategies and attempt alternative approaches, such as forming verbal associations, using multisensory approaches (such as 'talking through' visually demanding tasks), and using simultaneous versus serial processing of information. This aspect of cognitive remediation is much more therapist-dependent than the rote computerized drill and practice approaches, but likely a critical feature given the limitations of the latter approach with respect to duration and generalization of cognitive effects. Small group settings might also foster strategy development, as well as a secondary effect of social cognitive skills such as perspective taking, by hearing others' strategies and trying them during one's own performance.

Between-session application.

Based on the idea that training a skill does little good without information about applicability of the newly trained skills, some interventions have a structured curriculum aimed at application of the skills learned in everyday functional settings. These "bridging groups"¹ are a common feature of these interventions, although exactly what type of bridging is required is not entirely clear.

EXAMPLE COGNITIVE REMEDIATION PROGRAMS

Two programs have been widely used and a number of investigators have developed customized programs as well. We will describe these two programs because they are excellent examples of alternative approaches with proven success.

COG PAC. The COG PAC system was developed by Marker Software in Germany. This program uses an array

of different visually presented stimuli that tap executive functioning, processing speed, and other abilities, such as working memory. Thus, this is a top-down program and has to be customized to each user, as there are multiple different tasks, some of which (e.g., recognizing currency) do not appear to have cognitive enhancement potential.

Posit-Science Brain Fitness. The Posit-Science Brain Fitness program is produced by its distributor and provides a number of cognitive enhancing modules, including auditory and visual routines. In addition, there is a driving simulation module. Previous studies of this program with schizophrenia have used the auditory training routines, which were developed on the basis of research on the structure and function of the auditory cortex.³ This bottom-up approach aims to improve the signal-to-noise processing at the perceptual level.

A recent study compared the effects of the COG PAC and the Posit-Science Brain Fitness programs.⁴ Auditory perceptual training produced superior effects on a neurophysiological measure of sensory gating and verbal memory, suggesting that cleaning the perceptual filter in schizophrenia can lead to upstream effects on higher cognitive functions. Notably, however, the COG PAC treatment was less intensive and did not include many of the important strategies identified previously, such as strategic monitoring and bridging. Future studies might further examine how comparable doses of different programs and strategies might be more effective and efficacious considering healthcare costs and functional outcomes.

FUTURE APPLICATIONS

Although cognitive-enhancing strategies have used computers to

present stimuli and provide feedback for the past few decades, the field is far from full exploitation of technological advances. While the commercial market for brain training is backed by large corporations, the effects of cognitive exercise on nonimpaired populations is questionable, although methodology used to address this question⁵ has been remarkably poor. As mobile technologies and internet access become more common for those with serious mental illnesses, it would make sense to tailor these innovations to the populations that stand to benefit most from opportunities to supplement traditional cognitive remediation with more flexible exposure than can be offered in the office setting.

Outcomes improved by cognitive remediation. Although cognitive remediation is obviously aimed at cognitive processes, these processes are rarely the focus of clinical complaints and are targeted because of their functional implications. Thus, the goal of cognitive remediation is to improve everyday functioning, based on the widely accepted relationship between cognition and functional outcomes. As we have described in past columns, the influence of cognition on functional outcomes may occur through influences on functional capacity, the ability to perform critical everyday living skills.⁶ The NIMH-MATRICES consensus criteria for the evaluation of the efficacy of cognitive enhancement studies also suggests that “co-primary” measures of functional capacity are needed to thoroughly judge the benefits of cognitive enhancement therapies.⁷ Thus, cognitive remediation interventions should also be judged on the basis of improving functional capacity, in the absence of any long-term information about the ability of these interventions to improve everyday functioning.

Several studies, reviewed in a recent meta-analysis, indicated that cognitive remediation interventions led to more substantial functional gains when paired with a psychosocial intervention.⁸ For instance, a series of papers by McGurk et al⁹ describe the results of a study that demonstrated that cognitive remediation interventions improved vocational outcomes substantially. All patients in the study were currently receiving intensive vocational interventions. When cognitive remediation was added to a randomized subsample, their vocational outcomes were substantially improved compared to the sample who received standard treatment. Further, these outcomes were maintained at a three year follow-up. Thus, an average of 20 training sessions over a 13 week period led to persistent benefits. Of interest is the magnitude of the improvement, in that although the largest improvement on any cognitive measure was 0.4 standard deviation (SD) and the composite score improved by 0.25 SD, the patients who received the cognitive remediation earned 1,100 percent more money in the first 12 months with this benefit persistent at three years. Normalization of cognitive functioning is clearly not required in order to obtain substantial and persistent benefits in functioning from cognitive remediation.

OTHER BENEFITS OF COGNITIVE REMEDIATION

Additional studies have shown that cognitive remediation has potential central nervous system (CNS) effects. For instance, Vinogradov et al¹⁰ reported that patients who received cognitive remediation manifested an improvement in their serum levels of brain-derived neurotrophic factor (BDNF). While this is a peripheral measure, at the end of the treatment study, patients who received active

cognitive remediation manifested normalization in their BDNF levels while patients receiving the inactive treatment did not change at all.

In a study of cognitive remediation in dyslexia,¹¹ it was found that a structured intervention aimed at improving reading performance also lead to structural brain changes. Regional fractional anisotropy was improved in cases who received the treatment and manifested a beneficial treatment response. Thus, cortical white matter became more organized and coherent after remediation therapy.¹¹ As white matter changes in schizophrenia are a substantial source of interest, later research on improving cortical structural connectivity with cognitive remediation seems a likely prospect.

BARRIERS AND IMPEDIMENTS

One of the substantial barriers to cognitive remediation is pharmacological. As reported by Vinogradov et al¹² high levels of total anticholinergic burden were associated with reduced benefit from cognitive remediation. This should not be a surprising finding given the consistent correlations detected between memory impairments and high levels of circulating anticholinergics. This total anticholinergic burden does not come entirely from treatment with medications aimed at reduction of extrapyramidal symptoms. Many other medications also have substantial anticholinergic effects. Given the level of effort on the part of patients and service providers required to deliver cognitive remediation, consideration of reducing pharmacological impediments seems to be an important task.

Community success is also subject to multiple barriers and impediments. As previously found, patients with motivation to succeed, willingness to participate in training interventions, and opportunities to exercise their

TAKE HOME POINTS

1. Patients with schizophrenia benefit from cognitive remediation and their everyday functioning has been shown to improve with concurrent psychosocial interventions. Neither treatment alone seems to have similar efficacy.
2. Cognitive remediation causes neurobiological changes and has evidence of biological validity. The changes that occur do suggest evidence of activation of brain repair mechanisms.
3. Anticholinergic medications negate the benefit of cognitive remediation and other learning-based interventions. Their use should be kept to a minimum.

skills afterward appear to have the potential for sometimes substantial functional gains. Motivation and willingness may be associated with negative symptoms, which have shown in previous studies to exert an adverse influence on everyday functioning above and beyond that of cognitive limitations and reductions in functional capacity.¹³

Coming up short in any one of these domains has been shown to lead to markedly reduced chances of important functional gains. Opportunities seem the most difficult domain in which to intervene, because structural shortcomings in mental health treatment, such as lack of supported employment programs, cannot be remedied through individual interventions. Motivational interviewing as a strategy to increase motivation and increase willingness to participate in treatment has been

suggested in substance abuse and other conditions. Cognitive behavioral technique interventions can be aimed at the reasons underlying reduced motivation and willingness to participate. These interventions seem to be a needed prerequisite, because some individuals only attempt one training session before discontinuing.

REFERENCES

1. Medalia A, Revheim N, Herlands T. *Cognitive Remediation for Psychological Disorders, Therapist Guide*. New York, NY: Oxford University Press; 2009.
2. McGurk SR, Mueser KT, Pascaris A. Cognitive training and supported employment for persons with severe mental illness: one-year results from a randomized controlled trial. *Schizophr Bull*. 2005;31:898–909.
3. Adcock RA, Dale C, Fisher M, et al. When top-down meets bottom-up: auditory training enhances verbal memory in schizophrenia. *Schizophr Bull*. 2009;35:1132–1141.
4. Popov T, Jordanov T, Rockstroh B, et al. Specific cognitive training normalizes auditory sensory gating in schizophrenia: a randomized trial. *Biol Psychiatry*. 2011;69:465–471.
5. Owen AM, Hampshire A, Grahn JA, et al. Putting brain training to the test. *Nature*. 2010;465:775–780.
6. Green MF, Nuechterlein KH, Kern RS, et al. Functional co-primary measures for clinical trials in schizophrenia: Results from the MATRICS Psychometric and Standardization Study. *Am J Psychiatry*. 2008;165:221–228.
7. Buchanan RW, Keefe RS, Umbricht D, et al. The FDA-NIMH-MATRICS guidelines for clinical trial design of cognitive-enhancing drugs: What do we know 5 years later? *Schizophr Bull*. 2011;37:1209–1017.
8. Wykes T, Huddy V, Cellard C, et al. A meta-analysis of cognitive remediation for schizophrenia: methodology and effect sizes. *Am J Psychiatry*. 2011;168:472–485.
9. McGurk SR, Mueser KT, Feldman K, et al. Cognitive training for supported employment: 2 to 3 year outcomes of a randomized controlled trial. *Am J Psychiatry*. 2007;164:437–441.
10. Vinogradov S, Fisher M, Holland C, et al. Is serum brain-derived neurotrophic factor a biomarker for cognitive enhancement in schizophrenia? *Biol Psychiatry*. 2009;66:549–553.
11. Keller TA, Just MA. Altering cortical connectivity: remediation-induced changes in the white matter of poor readers. *Neuron*. 2009;64:624–631.
12. Vinogradov S, Fisher M, Warm H, et al. The cognitive cost of anticholinergic burden: decreased response to cognitive training in schizophrenia. *Am J Psychiatry*. 2009;166:1055–1062.
13. Leifker FR, Bowie CR, Harvey PD. The determinants of everyday outcomes in schizophrenia: Influences of cognitive impairment, clinical symptoms, and functional capacity. *Schizophr Res*. 2009;115:82–87.

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