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Editorial

Use of cognitive remediation to treat negative symptoms in schizophrenia: is it time yet?

Rafael Penadés and Til Wykes

Cognitive remediation is currently recommended to treat cognitive and functional impairments in patients with schizophrenia. Recently, treatment of negative symptoms has been proposed as a new target for cognitive remediation. Evidence of reductions in negative symptoms has been described in different meta-analyses. However, treating primary negative symptoms is still an open question. Despite some emerging evidence, more research focused on individuals with primary negative symptoms is indispensable. In addition, more attention to the role of moderators and mediators and the use of more specific assessments is necessary. Nevertheless, cognitive remediation could be considered as one promising option to treat primary negative symptoms.

Keywords
Schizophrenia; cognitive–behavioural therapies; rehabilitation; psychotic disorders; individual psychotherapy.

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Treating cognition and functioning

Over the past two decades more than 20 meta-analytic studies have investigated cognitive remediation therapies and have demonstrated benefits for people with a diagnosis of schizophrenia and psychosis. Most show significant improvements not only in cognition but also in psychosocial functioning. Despite this overwhelming evidence of positive effects, it is only recently that clinical practice guidance has included this treatment in their recommendations. Drop-out rates also suggest that cognitive remediation is acceptable and well tolerated[1] and important adverse effects are yet to be noticed.

Despite treatment recommendations, and efficacy and acceptability information, there still seem to be barriers hindering cognitive remediation implementation into services around the world. Examples include therapist training, and policy and service commitment so treatment availability will take some time before being offered to any patient who might benefit. The cost-effectiveness balance is probably another noteworthy deterrent although the cognitive benefits have been shown to be related to lowered community and hospital costs. Recent data also suggests that for a quality-of-life-year improvement that the cost is less than £5000, much lower than the UK National Institute for Health and Care Excellence (NICE) £20 000 threshold for adopting a treatment.[2]

Treating negative symptoms

Recently, a new indication for cognitive remediation has been tentatively proposed – negative symptoms. Some international guidance, such as the American Psychiatry Association or NICE, did not consider treating negative symptoms with cognitive remediation, but the recent European Psychiatry Association (EPA) guidance has.[3] Based on meta-analytic results and other evidence, the EPA made two recommendations:

(a) those with negative symptoms and cognitive difficulties – a resounding 'yes', offer treatment; and
(b) for those individuals with schizophrenia who have primary negative symptoms – 'no specific recommendation can be given'.

The difference was based on the lack of trials testing the effect of cognitive remediation on patients with only primary negative symptoms. The EPA relied on evidence from a high-quality meta-analysis involving 2500 participants from different countries and settings that demonstrated that cognitive remediation has a positive effect on negative symptoms.[4] That meta-analysis and the one by the same group, included in this issue (Cella et al[5]), demonstrated that the cognitive remediation effect on negative symptoms was the same as available pharmacological and behavioural interventions designed to tackle negative symptoms directly.

In our opinion, cognitive remediation should already be considered among the most promising options to treat primary negative symptoms. However, some important questions need to be clarified. For instance, although the meta-analysis from the Cella group[3] reported moderate effects for negative symptoms, another recent meta-analysis[1] reported minimal to small effects. The differences could be because of different measurement of negative symptoms. Future studies need to focus on primary symptoms as a main outcome to generate comparable data and account for the role of moderators and mediators of treatment effects to better understand mechanisms of change. The effect on negative symptoms does not seem to be accounted for by poor methods, as the higher effects were found in trials with better methods.[4] The type of cognitive remediation might also have an effect as the larger effects are also found in those formulated to increase problem-solving strategies and that improve self-efficacy. These results must encourage more focused research and a more detailed analysis of cognitive remediation effects on reductions in negative symptoms.

Most published studies have not differentiated patients with primary or secondary negative symptoms. Although we would want to encourage those studies, we know that establishing the primacy of negative symptoms is not an easy task for either researchers or clinicians. It would be helpful to define the

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nature of negative symptoms as predominant, persistent or primary. Most studies use the Brief Psychiatric Rating Scale or Positive and Negative Syndrome Scale, but perhaps this practice needs to change to include new and more specific scales such as the Brief Negative Symptom Scale, the Clinical Assessment Interview for Negative Symptoms or the Negative Symptom Assessment Scale. These scales could provide more precise information on the nature of the negative symptoms and allow us to understand the cognitive remediation effects on different dimensions.

If we want to improve cognitive remediation effects, we need to understand its mechanisms of action. Little information about potential moderators that may contribute to negative symptom reduction is available in the literature even though these may explain the differences in effects and help build a more effective therapy. Psychological treatments are also affected by what is known as the common effects in psychotherapy and as cognitive remediation is often implemented together with other evidence-based recovery treatments it is sometimes unclear whether cognitive remediation has a specific and unique effect on aspects of negative symptoms. The cognitive remediation active ingredients have been identified for improving cognition and functioning,[1] but we do not know if those same active ingredients or mechanisms of change are relevant when the target is negative symptoms. Different pathways are possible for different outcomes so we need well-powered studies focusing on underlying processes and active cognitive remediation components to understand both the change mechanisms, and the cognitive remediation format effect to increase benefit.

Is it time yet?

Although treating primary negative symptoms is still an open question, cognitive remediation should be considered as a first-line treatment for improving cognition and functioning. For the future we already know that different psychological treatments show significant effects on negative symptoms, but the review by Cella *et al*[5] stressed that the methodology of the cognitive remediation studies suggests that cognitive remediation effects are more robust compared with the other approaches. The current available evidence therefore positions cognitive remediation as a strong candidate for reducing the severity of negative symptoms whether primary or secondary. Despite this there is still an urgent need for randomised controlled trials with patients presenting with primary negative symptoms that both use more specific negative symptoms scales and can account for the role of moderators and mediators in the treatment effects.

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