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Cognitive remediation – where are we now and what should we do next?

Summary

Although we have evidence that cognitive remediation is effective we have not yet persuaded service providers to adopt it into their treatment packages. This paper outlines the cognitive remediation literature that has sculpted the field. It is not a systematic review but an expert's opinion of the research required to influence treatment decisions so that our patients are offered the best options for fulfilling their goals. The gaps in research include defining the benefits in terms of those that service providers and service users value. These include costs against the effects of treatment and fulfilling individual recovery goals. These are not rocket science and only require extra and least burdensome (on participants) measures to be added to studies. We also need to use data we already possess to carry out further analyses to indicate how different therapies work and to compare across studies in large individual participant level databases.

Key words

Cognitive remediation therapy • Schizophrenia • Cognitive deficits

Cognition has always been thought to be important in a diagnosis of schizophrenia and particularly the effect that cognition has on perceptions, comprehension and in the development of acute symptoms such as hallucinations and delusions. Even 50 years ago individuals with a diagnosis of schizophrenia interviewed in pioneering studies of service user experiences described how their cognitive difficulties interfered with everyday cognition and mentioned, memory, sustained and divided attention as well as their overall concentration¹. Following these studies further research highlighted cognition as a “stable vulnerability” factor after noting that cognition was poor even between episodes but was worse in an acute episode of the disorder. Further studies, including my own²⁻⁴ then demonstrated that cognition predicted the limits of rehabilitation with those with poorer cognition having much less independence in their recovery. This research provided an essentially pessimistic view which suggested that cognition was intimately linked to psychosis and that the effects were widespread. Medical treatments seemed to have no impact. Then cognitive remediation appeared. Twenty odd years after the first studies there is now a growing and optimistic view of the potential for cognitive remediation to provide real benefits in terms of boosting recovery goals. The field is thriving. In a search of studies of cognitive remediation between 2014 and 2017 there were 76 trial reports in schizophrenia and 113 in non-schizophrenia disorders. But what exactly have we learnt and should we be paying more attention not just to trial quality but to factors such as the moderators and mediators of outcome.

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Is cognitive remediation useful?

Here I am quoting from the Cognitive Remediation Experts Workshop which in 2012 defined it as “is an intervention targeting cognitive deficit

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 everyday functioning". The key words are that we use scientific learning principles derived from psychological and educational research. People with the diagnosis also value improvements in cognition but we also need to be mindful that their expressed goals are often about functioning, and hence the addition of the goal of improving functioning outcomes. Figure 1 shows the outcomes from a meta-analysis ⁵ showing that the cognition effect size is 0.45 and that this effect is not changed when considering only studies that had high quality methods. This meta-analysis also concluded that there was a benefit to functioning that was durable. Treatment guidance depends on empirical data showing benefit so most scientists would assume that this treatment would be in the guidance. However, there is disagreement on whether enough evidence exists, with differing views around the world. Some countries and US states mandate the treatment whereas others have been more reticent despite the current evidence. There is even a difference within the UK with Scotland including cognitive remediation and the English guidance excluding it. What is clear is that it is not just the evidence base that affects treatment acceptance but also market forces particularly in the area of so-called "brain training" programmes. Apart from a fine for false advertising by the Federal Trade Commission (FTC) there have also been two open letters and a review, all from academics, arguing the case for and against the effectiveness of brain training mostly in the healthy population. There is complete agreement with the FTC that there has been an over-selling of training benefits in the healthy population and some grudging acceptance that there may be some benefit in clinical populations. This public disagreement will make service providers wary of adopting a good psychological treatment because they think it may be a leisure activity. There have also been two well publicised negative studies of cognitive remediation in schizophrenia ^{6 7}. These studies rather than negating the current evidence are important in providing a context in which benefits can disappear. Both are similar in adopting a novel software programme with little prior information on benefit. In fact the Gomar study used a programme that had been used in dementia and autism with little effect. So there is the possibility that the programmes were not effective in any context. But the programmes look similar to those used in many other studies. The main difference in both studies was the inclusion of participants who were much older than those recruited to many of the other cognitive remediation studies. There is some evidence that age does reduce

the effect size ^{8 9} and this factor alone may have accounted for the disappointing effects.

The gold standard for measuring the likelihood of benefit is dependent on the meta-analyses of individual trials. There are now 19 in the literature following the 2011 Wykes meta-analysis ⁵. Of these only two did not find a cognitive and/or functioning benefit and four did not find a symptom improvement. The evidence now appears to be overwhelming and what is required is not proof that there is any benefit but advice on how to personalise or tailor treatment so that there is the best chance for an individual to show an improvement.

Is there evidence on boosting cognitive remediation benefits?

The Wykes et al. (2011) study ⁵ found no specific differences between therapies or studies that would indicate better cognition outcome. We do know that improving motivation might show effects ¹⁰, and that learning potential might influence cognitive outcomes ¹¹ but all these effects need further replication. The Wykes meta-analysis also showed that teaching information processing strategies rather than just practising tasks benefited functional outcomes. Studies such as those of McGurk and colleagues and Bell and colleagues ^{12 13} demonstrate that adding cognitive remediation to other rehabilitation programmes such as supported employment differentially improved outcomes. In fact, in the McGurk study people who had failed to get a job, despite wanting one, were randomised to receive either supported employment or supported employment plus cognitive remediation. Over a 24-month period those receiving the additional therapy were more likely to be competitively employed and to have been in employment for longer. In another study Chris Bowie ¹⁴ provided individuals with skills training alone, cognitive remediation alone or a combined group. He found cognitive improvements only when cognitive remediation was provided and few improvements when only skills training was provided even in skills training. The most benefit was produced when the two therapies were provided together.

It seems that cognitive remediation has an effect on cognition and the assumption is that this then has a knock on effect on skills training. But the analyses of whether the effects are linked are only just being carried out. For instance, Wykes et al. ¹⁵ tested whether cognitive benefits were linked to functional benefits in a study of supported, voluntary and competitive employment. Despite there being reasonable benefits to memory, flexibility and planning, only the planning measure was predictive of improved quality of work (the primary outcome). The improvement in planning only accounted for 15% of the variance leaving a hefty 85% to be accounted for in the direct effect of

cognitive remediation on outcome. So we are still unclear which cognitive domains should be targeted to improve particular functional outcomes. The obvious way to make a choice has been to look for correlations between cognition and functional outcomes but as we have seen in the previous study those correlations do not necessarily predict the right target. In fact, Reeder et al.¹⁶ showed in a trial that although there were correlations between memory and social functioning, changes in memory did not benefit social functioning. It was a change in an uncorrelated variable that seemed to have a large effect.

Do we know how to tailor treatment?

We do possess some knowledge of personal characteristics that could enable us to understand the beneficial effects. In terms of sociodemographic and non-clinical factors we have some evidence that older people provided with cognitive remediation for a similar amount of time as younger individuals show smaller benefits in terms of cognition^{8,9,17} We also know that some individuals show little benefit in terms of functional outcomes. For instance, a follow-up of a supported employment and cognitive remediation study¹⁸ two years after cognitive remediation, found there was no overall benefit in terms of employment status. However, if the group was divided into those with poor or better functioning at baseline a clear difference emerged. Those who had poor functioning at baseline showed a benefit from therapy two years later, but those whose functioning was higher did not seem to need the boost provided by cognitive remediation. In terms of treatment attributes, we know that pairing cognitive remediation with other rehabilitation services improves functioning and that providing a cognitive remediation programme which provides strategic teaching improves functioning. However, we do not know which cognitive domain we should target as many are reduced in those with a diagnosis of schizophrenia and that those same domain deficits are shown in both early and more chronic stages¹⁹. Targeting the domain that is most problematic has also not shown benefits as there was no difference in a targeted therapy and a more general approach in a large trial in France²⁰.

So there is a lot we do not know. We do not, for instance, know if maintaining therapy gains by repeating sessions after the main therapy has ended will maintain benefits over longer periods of time, or whether increasing the number of sessions for those who are more chronic will boost therapy gains. It is likely that a more general rather than a focussed approach would be appropriate at this stage, as it is unclear whether there is only a benefit for cognitive domains that are problematic or whether functional improvements are gained with a strengthening of domains where performance is not so reduced. The main obstacle for all tailoring is an understanding of the mechanisms of change. There was hope that brain

imaging might help to unravel these complex mechanisms. Despite having evidence that cognitive remediation affects brain activation²¹⁻²⁴ the modulation of activation and connectivity^{25,26}, structural integrity²⁷ and the prediction of outcome²⁸ we still do not know if these effects are replicable and they do not provide much information on how to change therapy ingredients or choose the individuals who will receive a benefit. In particular, there are individual differences in the way that tasks are approached that entirely explain the brain imaging results (e.g.²¹). The causal gap in neuroscience has recently and cogently been described by Etkin²⁹. Until we have better data these studies although interesting do not offer much information to direct research in cognitive remediation.

Currently there is little rigorous evidence on which to make decisions on who to exclude from therapy or how to provide therapies. Personalisation of therapy will therefore still depend on a clear case formulation where individual goals are set and an appropriate cognitive remediation programme is provided. It is unlikely that any identified variable can offer much benefit in terms of personalisation as the list has neither been replicated nor been tested for its predictive properties across different therapies and different populations. That should be one of the tasks for the next period of research.

What is the goal of cognitive remediation therapy?

Cognition

What individuals with a diagnosis of schizophrenia want is to attain their recovery goals and ensure that the benefits last a long time. One of the issues is to understand how we measure outcome. Some time ago Wykes and Huddy³⁰ pointed out that the choice of cognition measures affects whether there is a significant effect. For instance, if two people differ in their performance on an outcome then it will be easier to show an improvement in the person who has poorer performance than one whose performance is average. This is a particular concern when performance is measured on a very narrow measure such as those produced by the CNTRICS consortium³¹. This allows very specific information to be extracted on the effects on particular cognitive domains. However, more general, sometimes called “dirty”, measures which rely on several cognitive domains to achieve good performance, will provide a clearer view of efficacy for a large number of people and it could be argued that this approach delivers stronger evidence for treatment implementation decisions. We also may be taking a “shoot yourself in the foot” approach to measuring some cognitive outcomes. Performance in planning tests is often determined by time-dependent measures. If a person is taught to plan, they are likely

to slow down and therefore not complete as many tasks within the allotted time or the time taken is longer although errors are reduced. In these situations, the speed-error trade-off is likely to leave individuals with the same score or an even lower score despite learning to plan more efficiently. This feature is more likely to occur in treatments emphasising strategy learning but has happened in studies where attention was trained. In one study despite finding no effect of training on cognitive measures there was an effect on functioning³².

Functioning

Although people with schizophrenia notice and value improvements in cognition³³, it is functional benefits that feature as recovery goals. Life skills, employment, relationships as well as housing have all featured in reports of goals³⁴. Here too we have problems in what would be the correct measure to use. Cognitive improvements might impinge on many different areas of functioning and these are also affected by the opportunity to practice new skills. This lack of opportunity has spurred researchers to adopt interim measures such as functional capacity measures. Although these provide some information on new learning often studies do not find close relationships between these capacity measures and actual performance. It is also actual performance that drives treatment implementation. So despite the extra efforts required to collect data from informants or in the field and the length of follow-up to determine change, the balance between the quick fix capacity measure and actual performance still favours measuring outcomes of value to individuals with the disorder.

We know that we can boost functional outcomes but are these benefits maintained. Certainly my own experience which has mainly been without being paired with other rehabilitation, has shown that maintenance of treatment effects on functioning without some extra rehabilitation is hard to achieve^{35 36}. One recent Italian study suggested that cognitive remediation did boost the outcome from standard rehabilitation but although cognitive outcomes were stable over time, the treatment arm that maintained functional improvements was one where cognitive remediation was paired with standard rehabilitation which was provided for an extended period of 12 months³⁷. Those in the study arm which provided less standard rehabilitation did not see those benefits.

Treatment implementation

The variation in implementation around the world is not just dependent on clear outcomes. It is also driven by a lack of information on the cost-effectiveness of treatment. All clinical services need to make decisions about how to spend their resources and if the choice is to spend it on cognitive remediation or not then there needs to be a good case made as there is an opportunity cost attached to this decision. We know that those individuals

with cognitive problems are more highly dependent on psychiatric and residential services³⁵ and that cognitive difficulties are related to these costs, i.e. those with more cognitive problems use more and higher cost services³⁸. Cognitive remediation provides value in terms of improving the outcomes of supported employment and reducing failure, especially for those with poor functioning at baseline. This is a cost saving which has not so far been calculated. A novel study linking cognitive remediation with cognitive behaviour therapy (CBTp)³⁹ discovered that those receiving supportive therapy or cognitive remediation prior to CBTp were no different in their levels of symptoms at the end of the trial. However, those who had received cognitive remediation achieved this level in fewer sessions. As CBTp requires more expensive therapists with a longer training programme this study suggests that there might be a potential cost saving. A few other studies have contributed to the evidence base on costs. The first of these studies was by Reeder et al.⁴⁰ demonstrated a saving in both residential and day care services at follow-up which was related to cognitive improvements after cognitive remediation. More recently, Vita et al.⁴¹ in Italy has shown a reduction in the number and length of admissions and Garrido et al.⁴² in Spain have shown reductions in both emergency and admission costs. The evidence base for the benefits in terms of costs is therefore growing and should be part of new trial outcomes.

Conclusions

Cognitive remediation does provide positive outcomes. We need to investigate the benefits of individual therapies against each other in order to understand their different benefits and costs. Some of these analyses can be carried out within large participant level databases and the National Institute for Mental Health has developed such a platform called the Database of Cognitive Training and Remediation Studies which has uploaded randomised trials of cognitive remediation at the participant level⁴³. These data will provide more data to test mechanisms as well as allowing between-therapy comparisons of potential predictors of outcome and therefore allow us to develop a set of variables for tailoring treatments. But if we are to implement therapy we need to persuade both service users and providers of the benefits. For this we need real outcomes valued by our clients which include recovery goals and the cost-effectiveness of treatment. Both are of interest as cognitive remediation requires commitment from providers and users who may well consider other therapies of more benefit.

Conflict of Interest

None.

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