Cognitive remediation in schizophrenia: background, techniques, evidence of efficacy and perspectives

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Impairment of cognitive functions is a core feature of schizophrenia with relevant consequences on patients’ psychosocial functioning. Cognitive remediation techniques have been recently developed with the aim to restore or compensate for such impairments and improve the functional outcome of the disease. There is now convincing evidence of the efficacy of many of these techniques, especially when delivered in the context of a comprehensive treatment programme. Whether the application of these techniques in the early phases of the disease could modify the disease course and outcome and how they could affect brain plasticity and the trajectory of brain disease of schizophrenia is still under scrutiny.

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Impairments in a wide range of cognitive abilities have been reported in up to 98% of patients with schizophrenia (Keefe et al. 2005). In recent years, the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) project has identified seven distinct cognitive domains that are consistently impaired in patients with schizophrenia: speed of processing, attention/vigilance, working memory, verbal and visual learning, reasoning and problem solving and social cognition (Nuechterlein et al. 2004). Furthermore, several studies have shown that both neurocognitive and social cognitive deficits are related to social impairment and poorer outcomes in different functional domains of schizophrenia (Medalia & Saperstein, 2013). There is increasing evidence that the core of such cognitive deficits may stem from neurodevelopmentally mediated alterations in brain plasticity (Kaneko & Keshavan, 2012). Although antipsychotic drugs are effective in reducing the symptoms of schizophrenia, cognitive impairments have mostly been found to be scarcely responsive to such treatments, with marginally better effects of atypical antipsychotics (Woodward et al. 2005). Given the relevance of cognitive dysfunctions and their

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poor response to pharmacological treatment, major initiatives are under way to find new non-pharmacological interventions for cognitive impairment in schizophrenia with the secondary aim to improve patients’ functional outcomes. Most such interventions are based on a large literature supporting the concept of brain plasticity and neurogenesis, the underlying theoretical framework deriving from a developmental neuroscience perspective which supports the idea that the brain is capable of changes and development throughout the lifespan (Kaneko & Keshavan, 2012). In this context, cognitive remediation attempts to improve and/or restore cognitive functioning using a range of approaches. Recently, a certain number of studies have shown that cognitive remediation is associated with neurobiological changes, providing evidence of activation of brain repair mechanisms during treatment (Kurtz, 2012).

Cognitive remediation for schizophrenia has been recently defined as ‘a behavioural training based intervention that aims to improve cognitive processes (attention, memory, executive function, social cognition or metacognition) with the goal of durability and generalisation’ (Cognitive Remediation Experts Workshop – CREW, 2010). There are two main models of cognitive remediation: ‘compensatory’ and ‘restorative’. The restorative model may utilize either a bottom-up or a top-down approach (Medalia & Choi, 2009). Cognitive remediation adopts various learning strategies that are applied differently in various methods of cognitive remediation, depending on whether they are primarily based on repeated execution of specific tasks or on the implementation of new strategies. In recent years, a number of cognitive remediation techniques, computerized and non-computerized, designed for individual or group settings, have been developed and adopted in the multimodal treatment approaches to schizophrenia.

The main structured protocols of cognitive training for schizophrenia are listed in Table 1.

Several quantitative reviews have indicated cognitive remediation interventions to be effective in reducing cognitive deficits and improving the functional outcome of schizophrenia (McGurk et al., 2007; Wykes et al., 2011). In their pivotal review on the issue, McGurk et al. (2007) showed that cognitive rehabilitation was associated not only with a moderate improvement of cognitive functions (effect size = 0.41), but also with a slightly less significant improvement of psychosocial functioning (effect size = 0.35). The most recent meta-analysis of controlled studies performed in schizophrenia (Wykes et al., 2011) showed a modest improvement in overall cognitive performance (effect size = 0.45), with some durability of the effects shown in follow-up studies after remediation (effect size = 0.43). There was also an effect on psychosocial functioning both at post-treatment (effect size = 0.42) and follow-up (effect size = 0.37) assessments. Both these reviews indicated that the most significant effects on social functioning can be achieved when cognitive training is administered together with other psychosocial rehabilitation programmes and when a strategic approach is applied. In any case, a growing literature indicates that cognitive training will most probably affect the functional outcome when individuals are given opportunities to practice the cognitive skills in ‘real world’ settings (Medalia & Saperstein, 2013). The effectiveness of different modalities of cognitive remediation embedded within a more comprehensive treatment programme in the naturalistic setting of care of Italian rehabilitative centres has been recently demonstrated (Vita et al., 2011). Cognitive remediation interventions have demonstrated effectiveness in reducing cognitive dysfunctions and improving psychosocial performance of subjects suffering from schizophrenia. Such effects are magnified, and probably more durable, if obtained within a more general integrated approach to the patient’s treatment. Treating cognitive deficits can be effective not only in adults with chronic schizophrenia, but also in the early course of the disease. Cognitive remediation could be considered as a potential tool to prevent or delay the onset of schizophrenia in a primary and secondary prevention framework (Barlati et al., 2012). Young patients in the prodromal phases of schizophrenia or with recent onset psychosis seem to exhibit a higher potential of recovery of their cognitive functions as compared with patients with fully manifested schizophrenia and it is conceivable that cognitive training may facilitate neuroplastic phenomena and may thus have a neuroprotective effect in these patients. In this perspective, cognitive remediation may have particular clinical usefulness within the ‘critical period’ for early intervention, thus offering a possible opportunity to alter the course of the disease and its functional outcome. Future studies should establish whether cognitive remediation may overcome the uncertain risk-benefit ratio and ethical concerns of prescribing antipsychotics to young people in the prodromal phase of schizophrenia or subjects ‘at high risk’ for psychosis (Ruhmann et al., 2009). Whether the application of these techniques could affect brain plasticity and the progression of cerebral structural and functional changes of schizophrenia is also to be further elucidated.

Further research should also address the cost–benefit ratio and practical applicability of cognitive remediation techniques in routine clinical practice, in order to assess whether their widespread implementation in mental health services may be recommended.
### Table 1. Structured protocols of cognitive remediation interventions for schizophrenia

<table>
<thead>
<tr>
<th>Cognitive training</th>
<th>Target</th>
<th>Duration</th>
<th>Setting (individual/group)</th>
<th>Computer assisted/not computer assisted</th>
<th>Restorative/compensatory</th>
<th>Drill and practice</th>
<th>Strategy coaching</th>
<th>Individually tailored</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPT</td>
<td>Cognitive functions, social skills and problem solving</td>
<td>Sessions of 60 min, 2–3 times a week (about 12 months)</td>
<td>Group (6–8)</td>
<td>Not computer assisted</td>
<td>Restorative</td>
<td>+</td>
<td>+</td>
<td>−</td>
</tr>
<tr>
<td>INT</td>
<td>Cognitive functions and social cognition</td>
<td>30 biweekly sessions, 90 min each one</td>
<td>Group (6–8)</td>
<td>Computer-assisted sessions and not computer-assisted sessions</td>
<td>Restorative</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>CRT</td>
<td>Cognitive functions</td>
<td>40 sessions at least 3 times a week, 45–60 min each one</td>
<td>Individual</td>
<td>Not computer-assisted session</td>
<td>Restorative</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Cogpack*</td>
<td>Cognitive functions</td>
<td>Sessions variables in duration and frequency (starting from 2 to 3 weeks)</td>
<td>Individual</td>
<td>Computer assisted</td>
<td>Restorative</td>
<td>−</td>
<td>+</td>
<td>−</td>
</tr>
<tr>
<td>CET</td>
<td>Cognitive functions and social cognition</td>
<td>Biweekly sessions (about 2.5 h every week) for 24 months</td>
<td>Group (couples and then groups of 3–4 couples)</td>
<td>Computer-assisted sessions and not computer-assisted sessions</td>
<td>Restorative</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>NEAR</td>
<td>Cognitive functions and problem solving</td>
<td>Sessions of 60 min, twice a week (about 4 months)</td>
<td>Individual/group (3–10)</td>
<td>Computer-assisted sessions and not computer-assisted sessions</td>
<td>Restorative</td>
<td>+</td>
<td>–</td>
<td>−</td>
</tr>
<tr>
<td>NET</td>
<td>Cognitive functions and social cognition</td>
<td>Sessions of 45 min at least 5 times a week (about 6 months)</td>
<td>Individual/group</td>
<td>Computer-assisted sessions and not computer-assisted sessions</td>
<td>Restorative</td>
<td>−</td>
<td>+</td>
<td>−</td>
</tr>
<tr>
<td>CAT</td>
<td>Cognitive functions</td>
<td>Variable (short weekly visits at home, lasting about 30 min)</td>
<td>Individual</td>
<td>Not computer assisted</td>
<td>Compensatory</td>
<td>−</td>
<td>−</td>
<td>−</td>
</tr>
</tbody>
</table>

Continued
<table>
<thead>
<tr>
<th>Cognitive training</th>
<th>Target</th>
<th>Duration</th>
<th>Setting (individual/group)</th>
<th>Computer assisted/not computer assisted</th>
<th>Restorative/ compensatory</th>
<th>Top-down</th>
<th>Bottom-up</th>
<th>Drill and practice</th>
<th>Strategy coaching</th>
<th>Individually tailored</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAR</td>
<td>Social cognition</td>
<td>12 sessions twice a week, 45 min each one</td>
<td>Small groups of two patients and a psychotherapist</td>
<td>Computer-assisted sessions and not computer-assisted sessions</td>
<td>Restorative/ compensatory</td>
<td>−</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>SCIT</td>
<td>Social cognition</td>
<td>24 weekly sessions, 50 min each one (about 6 months)</td>
<td>Group (6–8)</td>
<td>Computer-assisted sessions and not computer-assisted group sessions</td>
<td>Restorative</td>
<td>−</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>SCST</td>
<td>Social cognition</td>
<td>12 weekly sessions, 60 min each one (about 3 months)</td>
<td>Group (six patients)</td>
<td>Computer-assisted group sessions and not computer-assisted group sessions</td>
<td>Restorative</td>
<td>−</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>SCET</td>
<td>Social cognition, ToM</td>
<td>36 sessions of 90 min, twice a week (about 6 months)</td>
<td>Group</td>
<td>Not computer assisted</td>
<td>Restorative</td>
<td>−</td>
<td>+</td>
<td>+</td>
<td>−</td>
<td></td>
</tr>
<tr>
<td>MCT</td>
<td>Metacognition</td>
<td>8 biweekly sessions of 45–60 min (one cycle per month)</td>
<td>Group (3–10)</td>
<td>Not computer assisted</td>
<td>Restorative</td>
<td>+</td>
<td>−</td>
<td>−</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>SSANIT</td>
<td>Cognitive functions, social cognition and social skills</td>
<td>NT: biweekly sessions of 1 h SST: weekly sessions of 2 h Duration: 6 months</td>
<td>Individual (group)</td>
<td>NT sessions: computer-assisted SST sessions: not computer assisted</td>
<td>Restorative</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
</tbody>
</table>


*Cogpack is a typical computer-assisted cognitive remediation (CACR) technique.
The information acquired by future research on the mechanisms and effects of cognitive remediation could contribute both to improving our knowledge of the possibility to interfere with the trajectory of brain pathology of schizophrenia and to design new treatments for the disease that combine effectiveness and personalization.

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Conflict of Interest
None.

Ethical Standards
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References


