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The ultimate aim is to help the translation of most relevant research findings into every-day clinical practice. These contributions are written in house by the journal's editorial team or commissioned by the Section Editor (no more than 1000 words, short unstructured abstract, four key-words, one Table or Figure and up to ten references).

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 be 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 (Ruhrmann *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

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

Continued

Table 1. Continued

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

CAT, Cognitive Adaptation Training; CET, Cognitive Enhancement Therapy; CRT, Cognitive Remediation Therapy; INT, Integrated Neurocognitive Therapy; IPT, Integrated Psychological Therapy; MCT, Metacognitive Training; NEAR, Neuropsychological Educational Approach to Remediation; NET, Neurocognitive Enhancement Therapy; NT, Neurocognitive Training; SCET, Social Cognition Enhancement Training; SCIT, Social Cognition and Interaction Training; SCST, Social Cognitive Skills Training; SSANIT, Social Skills and Neurocognitive Individualized Training; SST, Social Skills Training; TAR, Training of Affect Recognition; ToM, theory of mind.

*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

The authors declare that no human or animal experimentation was conducted for this work.

References

- Barlati S, De Peri L, Deste G, Fusar-Poli P, Vita A (2012). Cognitive remediation in the early course of schizophrenia: a critical review. *Current Pharmaceutical Design* **18**, 534–541.
- Kaneko Y, Keshavan M (2012). Cognitive remediation in schizophrenia. *Clinical Psychopharmacology and Neuroscience* **10**, 125–135.
- Keefe RSE, Eesley CE, Poe M (2005). Defining a cognitive function decrement in schizophrenia. *Biological Psychiatry* **57**, 688–691.
- Kurtz MM (2012). Cognitive remediation for schizophrenia: current status, biological correlates and predictors of response. *Expert Review of Neurotherapeutics* **12**, 813–821.
- McGurk SR, Twamley EW, Sitzer DI, McHugo GJ, Mueser KT (2007). A meta-analysis of cognitive remediation in schizophrenia. *American Journal of Psychiatry* **164**, 1791–1802.
- Medalia A, Choi J (2009). Cognitive remediation in schizophrenia. *Neuropsychology Review* **19**, 353–364.
- Medalia A, Saperstein AM (2013). Does cognitive remediation for schizophrenia improve functional outcomes? *Current Opinion in Psychiatry* **26**, 151–157.
- Nuechterlein KH, Barch DM, Gold JM, Goldberg TE, Green MF, Heaton RK (2004). Identification of separable cognitive factors in schizophrenia. *Schizophrenia Research* **72**, 29–39.
- Ruhrmann S, Schultze-Lutter F, Klosterkötter J (2009). Intervention in the at-risk state to prevent transition to psychosis. *Current Opinion in Psychiatry* **22**, 177–183.
- Vita A, De Peri L, Barlati S, Cacciani P, Deste G, Poli R, Agrimi E, Cesana BM, Sacchetti E (2011). Effectiveness of different modalities of cognitive remediation on symptomatological, neuropsychological, and functional outcome domains in schizophrenia: a prospective study in a real-world setting. *Schizophrenia Research* **133**, 223–231.
- Woodward ND, Purdon SE, Meltzer HY, Zald DH (2005). A meta-analysis of neuropsychological change to clozapine, olanzapine, quetiapine, and risperidone in schizophrenia. *International Journal of Neuropsychopharmacology* **8**, 457–472.
- Wykes T, Huddy V, Cellard C, McGurk SR, Czobor P (2011). A meta-analysis of cognitive remediation for schizophrenia: methodology and effect sizes. *American Journal of Psychiatry* **168**, 472–485.