

Targeting social cognition to improve functional outcome of patients with schizophrenia: clinical evidences

R. Cavallaro^{1,2}, M. Bechi²,
M. Spangaro²

¹ Università Vita-Salute San Raffaele, Milan, Italy; ² IRCCS San Raffaele Scientific Institute, Department of Clinical Neurosciences, Milan, Italy

Summary

Social cognitive deficit is a key feature of schizophrenia, highly contributing to determine the functional impairment associated to the disease. Given the absence of effective pharmacological treatments, over the years several rehabilitative interventions targeting social cognition have been developed, with positive effects on patients' daily functioning and quality of life.

In this Manuscript we will discuss rehabilitative interventions adopted and designed at IRCCS San Raffaele Turro (Milan), with a specific focus on training targeting social cognition. Clinical evidences indicate that combined rehabilitation of both social cognition and neurocognition in schizophrenia deficit is able to lead to better improvements of the two components of cognition and functional outcome. The identification of all factors influencing functioning and outcome of rehabilitation, and the personalization of rehabilitative programs according to patient's cognitive and clinical profile will allow to maximize interventions' efficacy and to promote functional remission, which represents the ultimate goal of the treatment of schizophrenia.

Key words

Schizophrenia • Social cognition • Rehabilitation • Cognitive deficit

Introduction

Functional impairment represents one of the main features in schizophrenia, determined by both neurocognitive and social cognitive deficits ¹.

Patients often exhibit a low level of community functioning even prior to the onset of the first psychotic episode, generally worsening over the course of the illness.

Functional disruption is a treatment-refractory area of dysfunction in patients affected by schizophrenia ². Impairments in functioning manifest premorbidly and persist in remitted patients, often detectable in first-degree relatives of patients diagnosed with schizophrenia as well. Indeed, functional disability has been reported to be only marginally related to positive and negative symptomatology ³. Cognitive functions, such as verbal and visual learning and memory, working memory, speed of processing and attention, are strongly associated with daily functioning and are considered the most reliable predictors of functional outcome ⁴. However, taken together neurocognitive abilities are able to explain just the 20-30% of functional variability of patients with schizophrenia, suggesting that other elements may be involved ⁵.

In this context, social cognition has been proposed as the main mediator between neurocognition and daily functioning ^{6,7}. Social cognition represents the interface between emotional and cognitive processing, a multifactorial construct including the ability of individuals to understand themselves and others in the context of social interactions, such as others' thoughts, feelings and intentions ⁸.

Correspondence

Roberto Cavallaro
General Psychiatry Unit, Department of Clinical
Neurosciences, IRCCS San Raffaele,
Scientific Institute, via Stamira d'Ancona 20,
20127 Milan, Italy • Tel. +39 02 26433218
• Fax +39 02 26433265
• E-mail: cavallaro.roberto@hsr.it

Different studies showed that social cognition is associated with patients' quality of life and employment rate, considered indicators of "real-world" functioning⁹. Particularly, Theory of Mind (ToM), defined as the ability to infer other's mental states, and emotion recognition are two main components of social cognition and are highly correlated with functional domains and quality of life¹⁰. Studies including both neurocognition and social cognition reported a relationship between the two domains, also evidencing a stronger association of social cognition with functioning⁹. Social cognition is considered a more complex domain, requiring intact neurocognition as a 'necessary but not sufficient' condition².

As previously mentioned, social cognition has thus been proposed as the mediator between neurocognition and functioning¹¹. Different studies confirmed this hypothesis, although the specific interplay between the two components of cognition is not yet completely clarified¹².

Given the relationship between social and neurocognition and their impact on functional outcome, in recent years several integrated rehabilitative interventions have been developed¹³⁻¹⁵, showing that combined rehabilitation programs have a greater effect on functioning than single interventions¹⁶⁻¹⁸.

Rehabilitative interventions for patients with schizophrenia and related disorders at San Raffaele University Scientific Hospital, Milan

Rehabilitation of patients with schizophrenia and related disorders represents one of the main clinical and research fields of the Disease Unit for Psychotic Disorders at San Raffaele University Scientific Institute Hospital. Over the years, the synergy between clinical and research activity allowed to integrate and develop different new rehabilitative interventions, in order to offer increasingly effective and tailored rehabilitative programs. Rehabilitative programs are designed for both inpatients and outpatients, with differences between the interventions related to the different duration of the treatments, which are much longer for the latter. Rehabilitative programs for inpatients, with a mean duration of 1 month, usually consist in Standard Rehabilitation Therapy (described below) added to a short-term intensive (daily) Cognitive Rehabilitation Therapy (4 weeks). For clinically stabilized outpatients with schizophrenia the center offers clinical and psychological assistance, as well as complex individualized rehabilitative programs encompassing different interventions which are selected according to patient's clinical, neurocognitive, social cognitive and functional features.

Indeed, entering into rehabilitation programs requires careful and extensive evaluation through different

scales such as the Positive and Negative Syndrome Scale (PANSS), the Brief Assessment of Cognition in Schizophrenia, Wisconsin card sorting test, Quality of Life Scale, Theory of Mind Picture Sequencing Task and other more specific instruments for special research purposes.

A brief description of the different rehabilitative interventions adopted at San Raffaele Turro is listed below.

Standard rehabilitation program (SRT)

The SRT represents the start point of rehabilitation program. The intervention is focused on main community goals of social abilities, work, and autonomy, including subprograms from Integrated Psychological therapy (IPT Verbal Communication, Social Skill Training and Problem Solving), social skills training programs for residential, vocational, and recreational functioning, and psychoeducation.

Cognitive Remediation Therapy (CRT)

CRT consists in a Computer-aided training employing the Cogpack Software® (Marker, 1987-2007). This software includes different neurocognitive exercises that can be divided into domain-specific exercises, aimed at training specific cognitive areas known to be impaired in schizophrenia (verbal memory, verbal fluency, psychomotor speed and coordination, executive function, working memory, attention). Moreover, it also includes non-domain-specific exercises, which do not focus on one specific function but require the use of several functions at a time and engage functions such as culture, language and simple calculation skills. Most exercises are adaptive and the computer sets the level of difficulty, based on patients' performances during the session. The software records the performance of each patient for every session, giving the chance to receive feedback on both performance during the session and over the course of treatment, and allowing therapists to obtain a course profile of each patient. Usually CRT has a duration of 12 weeks (two 1-hour session/week). Neurocognitive improvements of CRT lead to moderate improvement of general functioning, however we observed that the improvements in daily functioning depend on the achievement of a cognitive profile as much as possible "normal", harmonious and balanced, supporting the idea that a qualitative leap in cognition is needed in order to gain an advantage in real life activities¹⁹. In a recent study we investigated the persistence of both cognitive and functional effects of combined cognitive remediation plus standard rehabilitation interventions, 5 years after completion of the intervention, also comparing different durations of the standard rehabilitation. Surprisingly, Results showed that cognitive abilities remained stable after 5 years in both groups, while functional performance significantly decreased in

patients treated with the 6 months intervention only. Data thus suggest that cognitive effects persist even after 5 years, while a longer standard rehabilitation following the cognitive remediation program may be needed to achieve a stable functional gain²⁰.

Social cognitive interventions

Social Cognitive Training (SCT)

SCT, designed and developed in our center, targets two different social cognitive abilities such as Emotion Processing (EP) and Theory of Mind (ToM). SCT is conducted by a trained psychologist over 12 weeks (one 1-hour session/week) on groups of about five members and made use of short videos selected from international cinema movies depicting human social interactions. In each session, two or three clips are showed and could be viewed several times, according patients' requests. Patients are then asked to become "social detectives", collecting every concrete and meaningful piece of information they notice and hypothesize interpretations of the scenes based on expressed emotions, relationships between characters, implicit motivations and mental states.

The efficacy of this training was confirmed in a recent study conducted by our team²¹ where patients included in SCT group were compared with both a cognitive remediation therapy plus standard rehabilitation (CRT) and an outpatients no treatment group (NT). All patients were assessed before and after treatment with a ToM, EP, and a neurocognitive evaluation. Results showed an improvement of ToM abilities in SCT group compared with CRT and NT, but no in EP. We observed also a smaller improvement of ToM ability among patients in control condition who participated to CRT, this result suggesting us that progresses showed by the SCT group are not only related to an unspecific effect of rehabilitation or to neurocognitive enhancement therapy but mainly to the SCT's effect.

Theory of Mind Intervention (ToMI)

ToMI, designed and developed in our center, is conducted by trained psychotherapists over five modules divided into 18 sessions (one 1-hour session twice a week) on groups of about 5 members using comic strips and cartoons depicting human social interactions. The modules are executed in ascending order of complexity, with the first three modules regarding cognitive ToM and the last two concerning affective ToM. Patients are then trained to recognize the relevant details, to collect every concrete and meaningful information, to read the verbal part of comic strips and to identify literal meaning. Patients have also to interpret hidden meaning using all the information collected and to hypothesize interpretations of scenes on

the basis of expressed emotions, relationships between characters, implicit motivations and mental states. Eventually, answers written by the patients are read aloud and discussed within the group. In a recent study we proved the efficacy of ToMI training compared to an active control group (newspaper discussion group, ACG)²². Before intervention, psychopathological, neuropsychological, functional and ToM assessments were conducted (baseline evaluation). Performances of interest (ToM) were re-evaluated after 3 months. Results showed an improvement of ToM abilities in ToMI, This improvement observed is not related to intellectual functioning or daily functioning of patients, although these variables correlate with basal ToM values.

In a further study¹⁶ we compared the effect of both ToMI and SCT versus NT on ToM abilities, confirming the efficacy of both training and observing no differences between groups.

Moreover in a recent study conducted by our group²³ we analyzed ToM improvement after treatment and clinical and demographic influencing factors on work abilities in a sample of patients attending to a work therapy group (WTG). WTG is designed for patients who previously had a job or are trying to obtain a new employment. WTG is conducted by rehabilitative therapists and is made up of 10 modules divided into: 1. Job/Work motivation; 2. Knowledge of previous working experiences and organization of curriculum vitae; 3. Assessment of patient's expectancies; 4. Assessment of residual resources; 5. Planning of interests and future possibilities; 6. Job interview strategies; 7. Possible problems in employment reality; 8. Substantial relationship problems managed with role-playing; 9. Submission of curriculum vitae and management of anxiety related to job wait; 10. Administration of bureaucracy related to job's contract and work reality. Interestingly, we reported that work outcome resulted significantly predicted by age at onset, neurocognitive abilities and the degree of ToM improvement after ToMI, thus further indicating the importance of an integrated rehabilitation program for patients with schizophrenia.

Emotion processing training

Deficits in emotion processing (EP) represent a target of rehabilitation in schizophrenia, as they have been related to poor personal and social functioning. We developed two treatments targeting EP, 1-hour sessions/week on groups of about five subjects²⁴. The emotion recognition by video group (ERV) training used short videos depicting human social interactions, selected from The Awareness of Social Inference Test (TASIT; McDonald, Flanagan, Rollins, & Kinch, 2003). We chose to use only the first part, the Emotion Evaluation Test, as training material, because it is designed to train interpretation

of naturalistic emotional display including facial movement, tone of voice and gestures (Fear, Anger, Sadness, Disgust, Surprise, Happiness and Neutral state). Before watching the video, patients were invited to pay attention to the signals listed above. A guided discussion about recognition of emotion expressed by the professional actors followed, with the goals to recognize: (1) which emotion was expressed by the actors, and (2) which elements facilitated understanding of the emotion (facial gesture, interaction among actors). If none of the participants chose the right emotion, the psychotherapist pointed out the emotional signals expressed in the video. In the emotion recognition by audio group (ERA) we used the same materials as those of the ERV training (TASIT part 1) but played only the audio, as suggested by the TASIT manual. Patients spent the first session identifying how emotions could be expressed in a dialogue listening to voices only, without seeing images. A guided discussion about recognition of emotion expressed by the professional actors followed, and the goals were to identify: (1) which emotion was expressed by actors, and (2) which elements facilitated understanding of the emotion (tone of voice, interaction among actors, topics and subjects discussed in the speech). If none reached the correct emotion, the psychotherapist pointed out the emotional signals expressed in the speech. Results showed a significant improvement in EP through the specific channel trained for both groups, with an extended effect also on vocal stimuli for the visual training group. Positive correlations were found between working memory, social functioning and EP. Our findings help to shed light on the possible different involvement of perceptual channels in schizophrenia, as well as supporting previous evidence that emotion recognition may be inter-related but does not overlap with neurocognition and can be specifically trained.

Metacognitive Training (MCT)

MCT, developed by Mortiz and colleagues, addresses several cognitive biases, including bias against disconfirmatory evidence (BADE), Jumping to Conclusion,

ToM and Overconfidence in Memory. The primary target of MCT is to modify the cognitive infrastructure of delusional ideation, improving patients' awareness of both the presence and dysfunctionality of cognitive distortions. MCT is conducted by trained psychotherapists on groups of 5 members. It is composed of eight modules, lasting 16 weeks (1 session/week). The modules deal with monocausal and unbalanced attributions, jumping to conclusions, belief in flexibility, deficits in theory of mind and social cognition, memory (overconfidence in errors), depression and low self-esteem. Interestingly, we reported that combining MCT with CRT can lead to greater improvements on BADE²⁵.

Conclusions

This overview on rehabilitative interventions strongly supports the importance and the need of integrated programs targeting both neurocognition and social cognition. Indeed, as we recently reported, psychosocial interventions targeting social cognition allows to achieve higher rates of recovery, that represents the ultimate treatment goal in schizophrenia²⁶.

Moreover, offering a broad range of different interventions allows personalizing rehabilitative programs according to patient's profile, thus maximizing treatments efficacy and promoting functional remission.

Beside cognitive functioning and psychopathology, other variables such as premorbid adjustment, genetic variability and pharmacological treatment are known to influence outcome of rehabilitation among patients with schizophrenia^{27,28}. The challenge of future research is to identify all factors influencing functioning and outcome of rehabilitation, and then to develop new integrated interventions. This would pave the way to higher rates of functional recovery of patients with schizophrenia, eventually reducing the psychosocial burden of the disease.

Conflict of Interest

None.

References

- Green MF. *Impact of cognitive and social cognitive impairment on functional outcomes in patients with schizophrenia*. J Clin Psychiatry 2016;77(Suppl 2):8-11.
- Fett AK, Viechtbauer W, Dominguez MD, et al. *The relationship between neurocognition and social cognition with functional outcomes in schizophrenia: a meta-analysis*. Neurosci Biobehav Rev 2011;35:573-88.
- Harvey PD, Green MF, Keefe RS, et al. *Cognitive functioning in schizophrenia: a consensus statement on its role in the definition and evaluation of effective treatments for the illness*. J Clin Psychiatry 2004;65:361-72.
- Keefe RS, Harvey PD. *Cognitive impairment in schizophrenia*. Handb Exp Pharmacol 2012;11-37.
- Green MF, Kern RS, Braff DL, et al. *Neurocognitive deficits and functional outcome in schizophrenia: are we measuring the "right stuff"?* Schizophr Bull 2000;26:119-36.
- Schmidt SJ, Mueller DR, Roder V. *Social cognition as a mediator variable between neurocognition and functional outcome in schizophrenia: empirical review and new results by structural equation modeling*. Schizophr Bull 2011;37(Suppl 2):S41-54.
- Hoe M, Nakagami E, Green MF, et al. *The causal relationships between neurocognition, social cognition and functional outcome over time in schizophrenia: a latent difference score approach*. Psychol Med 2012;42:2287-99.

- ⁸ Green MF, Horan WP, Lee J. *Social cognition in schizophrenia*. *Nat Rev Neurosci* 2015;16:620-31.
- ⁹ Bechi M, Bosia M, Spangaro M, et al. *Exploring functioning in schizophrenia: predictors of functional capacity and real-world behaviour*. *Psychiatry Res* 2017;251:118-24.
- ¹⁰ Brune M, Abdel-Hamid M, Lehmkamper C, et al. *Mental state attribution, neurocognitive functioning, and psychopathology: what predicts poor social competence in schizophrenia best?* *Schizophr Res* 2007;92:151-9.
- ¹¹ Addington J, Saeedi H, Addington D. *Influence of social perception and social knowledge on cognitive and social functioning in early psychosis*. *Br J Psychiatry* 2006;189:373-8.
- ¹² Brekke J, Kay DD, Lee KS, et al. *Biosocial pathways to functional outcome in schizophrenia*. *Schizophr Res* 2005;80:213-25.
- ¹³ Galderisi S, Piegari G, Mucci A, et al. *Social skills and neurocognitive individualized training in schizophrenia: comparison with structured leisure activities*. *Eur Arch Psychiatry Clin Neurosci* 2010;260:305-15.
- ¹⁴ Horan WP, Kern RS, Shokat-Fadai K, et al. *Social cognitive skills training in schizophrenia: an initial efficacy study of stabilized outpatients*. *Schizophr Res* 2009;107:47-54.
- ¹⁵ Hogarty GE, Flesher S, Ulrich R, et al. *Cognitive enhancement therapy for schizophrenia: effects of a 2-year randomized trial on cognition and behavior*. *Arch Gen Psychiatry* 2004;61:866-76.
- ¹⁶ Bechi M, Bosia M, Spangaro M, et al. *Combined social cognitive and neurocognitive rehabilitation strategies in schizophrenia: neuropsychological and psychopathological influences on theory of mind improvement*. *Psychol Med* 2015;45:3147-57.
- ¹⁷ Moritz S, Kerstan A, Veckenstedt R, et al. *Further evidence for the efficacy of a metacognitive group training in schizophrenia*. *Behav Res Ther* 2011;49:151-7.
- ¹⁸ Aghotor J, Pfueller U, Moritz S, et al. *Meta-cognitive training for patients with schizophrenia (MCT): feasibility and preliminary evidence for its efficacy*. *J Behav Ther Exp Psychiatry* 2010;41:207-11.
- ¹⁹ Bosia M, Buonocore M, Bechi M, et al. *Cognitive remediation and functional improvement in schizophrenia: is it a matter of size?* *Eur Psychiatry* 2017;40:26-32.
- ²⁰ Buonocore M, Spangaro M, Bechi M, et al. *Integrated cognitive remediation and standard rehabilitation therapy in patients of schizophrenia: persistence after 5 years*. *Schizophr Res* 2018;192:335-9.
- ²¹ Bechi M, Riccaboni R, Ali S, et al. *Theory of mind and emotion processing training for patients with schizophrenia: preliminary findings*. *Psychiatry Res* 2012;198:371-7.
- ²² Bechi M, Spangaro M, Bosia M, et al. *Theory of Mind intervention for outpatients with schizophrenia*. *Neuropsychol Rehabil* 2013;23:383-400.
- ²³ Bechi M, Spangaro M, Pigoni A, et al. *Exploring predictors of work competence in schizophrenia: the role of theory of mind*. *Neuropsychol Rehabil* 2017:1-13. [Epub ahead of print]
- ²⁴ Bechi M, Bosia M, Spangaro M, et al. *Visual and audio emotion processing training for outpatients with schizophrenia: an integrated multisensory approach*. *Neuropsychol Rehabil* 2016:1-14. [Epub ahead of print]
- ²⁵ Buonocore M, Bosia M, Riccaboni R, et al. *Combined neurocognitive and metacognitive rehabilitation in schizophrenia: effects on bias against disconfirmatory evidence*. *Eur Psychiatry* 2015;30:615-21.
- ²⁶ Buonocore M, Bosia M, Baraldi MA, et al. *Achieving recovery in patients with schizophrenia through psychosocial interventions: a retrospective study*. *Psychiatry Clin Neurosci* 2018;72:28-34.
- ²⁷ Buonocore M, Bosinelli F, Bechi M, et al. *The role of premorbid adjustment in schizophrenia: focus on cognitive remediation outcome*. *Neuropsychol Rehabil* 2018:1-14. [Epub ahead of print]
- ²⁸ Bosia M, Zanoletti A, Spangaro M, et al. *Factors affecting cognitive remediation response in schizophrenia: the role of COMT gene and antipsychotic treatment*. *Psychiatry Res* 2014;217:9-14.