

Integrated neurocognitive therapy in chronic schizophrenic inpatients: preliminary data and considerations

Terapia neurocognitiva integrata in pazienti psichiatrici cronici residenziali: dati preliminari e considerazioni

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SUMMARY. Background. The present paper aims at studying the efficacy of the Integrated Neurocognitive Therapy (INT), according to Roder's model, in a group of chronic schizophrenics in a long term residential condition. This kind of treatment is particularly interesting because, according to the most recent studies concerning schizophrenia as a neurodevelopmental disorder, allows to act on the neuro- and socio-cognitions areas, which are the most deteriorated ones. Moreover the INT program includes also computer aided activities (Cog PacK), which largely proved their efficacy on neurocognition. **Materials and methods.** The study sample consists of 10 inpatients suffering of Schizophrenia (according to DSM-5), 5 Male and 5 Female, average age 52, disorder average length 24,9 years, with IQ not <80. The sample took part in the 18 months INT program and has been evaluated through the neurocognitive set RBANS and MCST (modified version of WCST for the survey of the executive functions: abstraction, categorization, set shifting at the beginning of the treatment (T₀), after 12 months (T₁), and at its end, after 18 months (T₂). **Results.** As regards neurocognition, starting from the preliminary result analysis, the only statistical significance refers to time factor concerning the immediate memory measured by RBANS at T₂. We can also point out an improvement trend in T₁ evaluations for the single cognitive functions and for the general cognitive profile. Concerning the executive functions (MCST), even without any statistical significance, a general improvement trend is present (completed categories, persisting and not persisting mistakes). **Conclusions.** The data presented, even in a numerically reduced sample, encourage however an optimistic perspective concerning the INT rehabilitation use in schizophrenic inpatients, substantially confirming the data already present in literature. We have to pay specific attention even in the evaluation of computerized programs, whose use can aid the general sociocognitive functioning. We hope that later and wider studies will support what we have herein preliminarily presented and discussed.

KEY WORDS: Integrated Neurocognitive Therapy, schizophrenia, inpatients, computerized interventions.

RIASSUNTO. Background. Il presente lavoro si propone di approfondire l'efficacia della Terapia Neurocognitiva Integrata (INT) secondo il modello di Roder in un gruppo di schizofrenici cronici in condizione di residenzialità a lungo termine. Questo tipo di trattamento appare particolarmente interessante perché, nell'ottica dei più recenti studi relativi alla schizofrenia come disturbo del neurosviluppo, permette di agire sulle aree neuro- e socio-cognitive, che sono quelle maggiormente deteriorate. In più, il programma INT prevede l'uso di attività assistite con il computer (Cog Pack), anch'esse con comprovata efficacia sulla neurocognizione. **Materiali e metodi.** Il campione dello studio è formato da 10 pazienti affetti da schizofrenia (diagnosi DSM-5), di cui 5 M e 5 F, età media 52 aa, durata media di malattia 24,9 aa, con Q.I. non <80, in situazione di residenzialità a lungo termine. Il campione ha partecipato per un periodo di 18 mesi al programma INT ed è stato valutato tramite la batteria neurocognitiva RBANS e MCST (versione modificata del WCST per l'indagine delle funzioni esecutive: astrazione, categorizzazione, set shifting) all'inizio del trattamento (T₀), dopo 12 mesi (T₁) e alla fine dello stesso, dopo 18 mesi (T₂). **Risultati.** Per quanto riguarda la neurocognizione, dall'analisi dei risultati preliminari l'unica significatività statistica riguarda il fattore tempo, relativamente alla memoria immediata misurata con la RBANS a T₂. Si evidenzia anche una tendenza al miglioramento nelle valutazioni T₁ per le singole funzioni cognitive e per il profilo cognitivo generale. Relativamente alle funzioni esecutive (MCST), pur in assenza di significatività statistica, è presente una generale tendenza al miglioramento (categorie completate, errori perseverativi ed errori non perseverativi). **Conclusioni.** I dati presentati, pur nel limite di un campione numericamente ridotto, consentono però un'ottimistica visione relativamente all'impiego nella riabilitazione di soggetti schizofrenici in condizioni di residenzialità a lungo termine della INT, confermando sostanzialmente i dati presenti in letteratura. Particolare attenzione va posta anche alla valutazione dei programmi computerizzati, il cui utilizzo può aiutare il funzionamento sociocognitivo generale. È da auspicare che successivi e più ampi studi concorrano a supportare quanto qui preliminarmente presentato e discusso.

PAROLE CHIAVE: Terapia Neurocognitiva Integrata, schizofrenia, pazienti residenziali, interventi computerizzati.

INTRODUCTION

The evidences confirm how the neurocognitive deficit is central in schizophrenia¹⁻⁷, a disease that should be considered as a neurodevelopmental disorder too^{8,9}. In addition to the standard pharmacological practice, also cognitive therapies are recognized as an effective tool for psychiatric patients to acquire psychosocial and working skills and recover good social integration¹⁰ together with satisfactory and self-sufficient quality of life¹¹.

Trials incorporating cognitive training in treatment of schizophrenia cognitive deficits began more than 20 years ago, obtaining significant improvements¹².

Most of the training cognitive programs for schizophrenia are more frequently used to recover neurocognitive deficits better than social cognition¹³. Literature reviews point out how social and neurocognitive interventions promote a general improvement in real world functioning, but stress also the difficulties in having methodological accuracy, in small sample sizes, in results depending on the specific outcome measures chosen, etc.^{14,15}.

Also the influence of new technologies in social cognitive interventions must be considered, such as computerized programs which offer the possibility to gradually deal with exercises reproducing the problem of real life¹⁶.

The Integrated Neurocognitive Therapy (INT) for schizophrenia

Usually the rehabilitative social and neurocognitive approach shows its best results particularly in the psychotic onset^{3,17}. In the 35 papers examined in Grant's review on social cognition interventions methodology the 66% of patients included had an average age of 36, only seven studies included inpatients and the average ill duration was 13.4 years¹⁸. Several authors confirm positive effects also on "aged" patients¹⁹.

The INT¹⁴⁻²⁰ is an evolution of the Integrated Psychological Therapy, which has been influenced by the National Institute of Mental Health (NIMH) MATRICS (Measurement and Treatment Research to Improve Cognition in Schizophrenia) initiative²¹. MATRICS has pointed out the seven key-cognitive domains in schizophrenia able to be improved by specific interventions. These domains are: speed in information processing, attention/wakefulness, working memory, verbal learning, visual learning, reasoning and problem solving, and social cognition.

One of the INT fundamental aspects is the possibility to associate to the program a PC-based cognitive training (COG-Pack). The COG-Pack includes exercises for attention, psychomotor speed, learning and memory, executive functions, concentration, logical abilities and verbal reasoning. Computerized cognitive interventions have become more popular in the last years. As M. Fisher writes "an active area of schizophrenia research is to understand how to build upon prior work in the field in order to best design efficient computer-based cognitive-training methods to harness learning-induced neuroplasticity for improving neural system functioning and clinical presentation, and to prevent, and possibly even reverse, disease progression"²².

COG Pack exercises work on cognitive functions (attention, psychomotor speed, learning and memory, and executive functions). The first six sessions operate in all cognitive

domains, while the succeeding are concentrated on repeating the exercises in all the domains²³.

There are different forms for each exercise, which can be modified and enlarged. Also the sequence can be modified. Adaptive possibilities are present.

COG Pack program includes some basic exercises programmed to allow the patients to learn PC use. Most of the sample had no confidence with PC, and need these introductory exercises.

INT method is made of both restorative and compensatory approaches to deal with the schizophrenia most important social and cognitive deficits. This is one of the main differences compared to other cognitive trainings, more concentrated only on one or the other of the two aspects²⁴.

Inpatients and schizophrenia

The long term residency is one of the main problems in current psychiatric assistance. Since 1952 Maxwell Jones spoke about the function of psychiatric residency based on the concept of "learning living situation and sensitive training" and as a basis for the change process produced by the community life²⁵. Very often the residential center is just a container of psychiatric group rehabilitation activities, with no particular attention to the housing. But psychiatric rehabilitation needs also everyday life experiences, to reach a renewed reality approach. To avoid self-referentiality, decontextualisation related to the regular social life and to the possibility of restarting it, INT program allows chronic inpatients to immerse themselves in social and neurocognitive rebuilding activities suitable to get contacts with reality again. The aim of this paper is to investigate the effects of a neurocognitive group treatment associated to computerized intervention in chronic schizophrenic inpatients. It has been carried out in a long term psychiatric residential clinic.

MATERIALS AND METHODS

The study examines the results of the first 12 months of INT (T₀-T₁) without use of computerized program, the total period of INT submission (18 months, T₀-T₂) and the period when the COG-Pack has been added to the treatment (late six months T₁-T₂).

Sample

The sample included 10 patients meeting DSM 5 diagnostic criteria for Schizophrenia and Schizoaffective Disorder²⁶, 5 males and 5 females, age range 52, average illness duration 24.9, onset average 29. An I.Q. not lower than 80 was an inclusion criteria.

The characteristics of the patients group are reported in Table 1.

All the patients were on stabilized antipsychotic drug treatment since at least six months, without any substantial changes along the period of the observation. Each subject was submitted to an "inclusion interview", to verify her/his peculiar attitude to the intervention.

Treatment

The program, based on Roder's INT protocol, translated into Italian by Vita²⁷, started in December 2016 by the submission of Paradigm A and B. Paradigm A of INT is related to the therapeutic

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Table 1. Sample description.

Sex	Age (average)	Onset	Illness duration (years)
M: 5	47.8	31 y.o.	27
F: 5	56.2	27 y.o.	22.8
Tot: 10	Average: 52	Average: 29	Average: 24.9

tic neurocognitive area: information processing speed and attention/vigilance. Paradigm B consists of exercises for verbal and visual memory. The activity is carried out in groups of 5-6 patients, leaded by a therapist (psychiatrist) and a co-therapist (psychologist).

In the first 12 months of treatment the program was performed as planned in both paradigms (A and B): each session had an introductory part and a working one, using clinical illustrations, work sheets, movie clips, papers, projectable pictures as prescribed by Roder's procedure. The COG Pack was not introduced in this phase, aiming at the assessment of the results of the basal form of the treatment.

After the first 12 months, the Cog Pack exercises have been included in each working session too.

The sample described in this study worked on training about time management, attention, immediate and delayed memory, visuo-spatial abilities, language. Working in group allowed also to act on interpersonal relationships and relational dynamics. These aspects will be presented and discussed in a further paper.

Assessment and Statistics

The neuropsychological assessment was performed by the Repeatable Battery for the Assessment of Neuropsychological Status-RBANS²⁸ and the Modified Card Sorting Test (MCST)²⁹ administered at T₀ (baseline), T₁ (after 12 months treatment) and T₂ (after 18 months treatment). The MCST has been preferred to the usual WCST because of its simplified methodology, more useful for the investigated sample. To verify whether and how the INT rehabilitation program had influenced the cognitive mechanisms (i.e. attention, memory, visuo-spatial abilities, language) and the executive functions (abstraction, categorization and set shifting), the mean scores obtained in cognitive evaluations by RBANS and MCST at T₀, T₁ and T₂ have been compared by ANOVA for repeated measures in a single experimental group with "time" as factor with in two levels (pre- and post-rehabilitation treatment).

RESULTS

Regarding RBANS scale the results are:

T₀-T₁ (12 months)

The "time" factor for the cognitive functions of immediate memory (p=0.284), attention (p=0.547), visuo-spatial abilities (p=0.170), language (p=0.624), delayed memory (p=0.567) and total score (p=0.157) is not statistically significant. A trend towards improvement of the single cognitive functions and the general cognitive profile has been observed.

T₀-T₂ (18 months)

The "time" principal factor is statistically significant [F(1,9)=7.8584; p<0.05].

The higher scores obtained in immediate memory area could be considered related to the fact that during 18 months of treatment, the subjects have been submitted both to verbal and computerized INT parts (Figure 1).

In the same period the time factor is not statistically significant related to attention (p=0.722), visuo-spatial abilities (p=0.162), delayed memory (p=0.131) and total score (p=0.164), even if a trend towards improvement can be observed over time. It is interesting to stress that regarding language (p=0.628) the time factor is also not statistically significant, with a worsening after 18 months of treatment.

T₁-T₂ (6 months)

In the last six months of treatment (after COG Pack introduction into the program) the time factor is not statistically significant respect to immediate memory (p=0.115), visuo-spatial abilities (p=0.854), delayed memory (p= 0.198) and total score (p=0.910), even if a mild trend to improvement can be appreciated. Regarding attention (p=0.864) and language (p=0.257), there is not statistical significance, but a trend towards worsening has been observed.

About MCST the results are:

T₀-T₁ (12 months)

In the first year of treatment, the time factor is not statistically significant respect to the number of completed categories (p=0.144), but there is a positive trend towards improvement, since the number of completed categories shows a mild increase along the treatment period. Also the number of perseverative (p=0.6) and non-perseverative errors (p=0.468) are not statistically significant: the number of committed perseverative errors grows inversely to the non-perseverative errors, stressing a trend towards cognitive rigidity rather than a greater skill in self shifting.

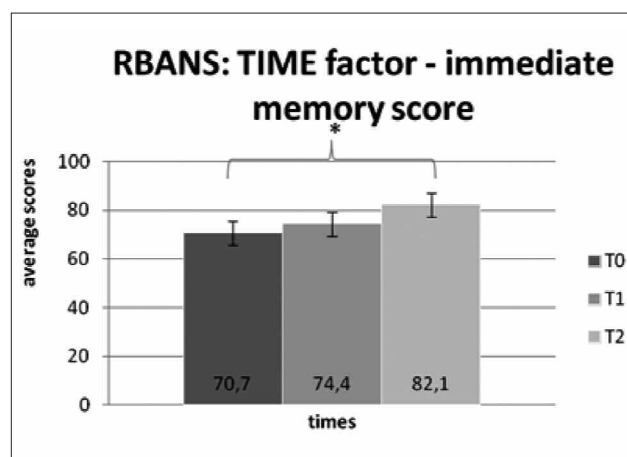


Figure 1. RBANS immediate memory score.

T₀-T₂ (18 months)

In the total period of treatment the time factor is not statistically significant related to the number of completed categories ($p=0.277$), but a positive trend towards improvement persists. Also the number of perseverative ($p=0.348$) and not perseverative errors ($p=0.378$) is not statistically significant, with a trend similar to that in the first 12 months of treatment. The total number of committed errors (i.e. perseverative errors + non perseverative errors) decreases after 18 months treatment, but it is not statistically significant ($p=0.303$).

T₁-T₂ (18 months)

In the last 6 months of treatment, the time factor is not statistically significant related to the number of completed categories (mean score =2,4; $p=0.455$): a mild worsening can be appreciated after the use of Cog Pack program, but (as pointed out by the analyses T_0 - T_2) there is however an improvement compared to the starting of INT program (respectively average score =2.0 and average score=2.2). The number of perseverative ($p=0.525$) and not perseverative errors ($p=0.955$) doesn't result statistically significant, with a trend similar to that in the previous analyses.

DISCUSSION

The results allow some considerations about INT protocol effectiveness on chronic schizophrenic inpatients. Broadly both RBANS and MCST scores assure a reasonable improvement in the main cognitive domains.

The statistically significant result is the RBANS assessment of immediate memory improvement related to the "time factor" after 18 months treatment. The immediate memory is the capacity to recover after few minutes the previously stored informations. Cirillo and Siedman's review suggests that schizophrenic patients hold less information back than the healthy controls (from 10% to 20% less)³⁰. So in people with schizophrenia a little but substantial part of the learned information storage ability is compromised. Therefore INT treatment seems to positively influence this capacity. Probably the better memory functioning could also be to some extent related also to the relaxing atmosphere and the collaboration mood among patients themselves and the therapists during the work sessions. These have been really stimulating for the patients, likely making them more efficient in using immediate memory.

Another reflection is due on the trend to worsening of language, both in T_0 - T_2 than in T_1 - T_2 comparisons.

It is well known that a lot of abnormalities have been described in schizophrenic language. It is often hard to define to what extent the anomaly is connected with the language itself and to what extent with cognitive processes impairment³¹.

In his study Wrobel suggests that schizophrenia is fundamentally a semiotic disorder³². The RBANS test structure appears not to consider language as verbalization skill, but it takes into account the naming capabilities. They regard the pragmatics and semantic field, i.e. the relationships between language and context. Thus it can be postulated that the se-

mantic disorder interferes with the competency in verbal production of a specific word through the executive functions. The final part of the protocol – not yet submitted to the patients – includes a series of more specific exercises for this ability. As a consequence we can hypothesize a further improvement in this area too. Moreover schizophrenic patients have a general difficult in cognitive flexibility such to influence the answers repetition, regardless of the test timing administration. Further evaluations are necessary to better interpret the results.

In the other cognitive fields explored by RBANS (visuospatial abilities and delayed memory) the scores changes are not statistically significant, but a mild trend towards improvement can be noticed and the small sample size may probably account for this.

The MCST assesses the ability in elaboration of abstract categories and the skill in changing category related to a temporary situation modification. The test goes forward by attempts and mistakes.

Schizophrenic patients usually perform poorly in this test³³.

In the present evaluation related to INT treatment the changes appear to be not statistically significant despite of a mild trend to change presence.

The number of completed categories tends to increase in the first 12 months, then (T_1 - T_2) a light worsening is observed. This last period is the treatment phase where Cog Pack has been inserted in the program. The first Cog Pack exercises used in the program were related to memory, attention and concentration and not to executive functions. Probably the minor working on executive functions has caused the worsening as compared to the first 12 months. This hypothesis should confirm the RBANS score regarding language results.

The perseverative and non-perseverative errors have not showed statistically significant scores. In the first 12 months the perseverative errors are more than the non-perseverative ones. This is in accordance with most of the literature which demonstrates how schizophrenic patients make more perseverative errors than healthy controls³⁴. We can hypothesize this result as related to the set shifting impairment. Over time also the total errors number decreases. It could be interpreted as a general improvement, where the imbalance towards perseverative errors is to the detriment of non-perseverative ones.

CONCLUSIONS

Some limitations of the study must be considered, potentially influencing its final results. The sample size is very small, since it was selected from a not large general population of inpatients meeting the inclusion criteria, according to the INT protocol, of specific diagnosis and sufficient I.Q. The small sample size has certainly limited the possibilities of the statistical analysis, also giving, in the meantime, some more clinical relevance also to not statistical trends. Because of the above mentioned situation, it has been not possible to have a control group. The lack of comparison doesn't nevertheless reduce the within group significance of the data and its possible relation to the clinical meaning of the results.

In conclusion, the results appear to confirm the potential importance of INT as an effective rehabilitation tool in schiz-

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ophrenia, suggesting its efficacy also in chronic inpatients. It is well known that these patients generally move towards a progressive cognitive and social functioning decline, progressively reducing substantial possibilities of an independent life³⁵. The possibility of maintaining or restoring sufficient cognitive abilities even if in a long term psychiatric residence may give them back, at least partially, the perception of being active part of their life and their recovery³⁶.

As emerged from above, in the long period the results in different cognitive and executive areas show a trend towards the improvement. It is important to stress that this work has had as subjects chronic psychiatric inpatients, who experience a situation of general deprivation, with poor affective, cognitive and social stimulations.

In these patients the final aim of rehabilitation work can also be mainly directed to preserve the basal level of social and cognitive functioning, so to avoid the deterioration connected with schizophrenic disease.

Further studies and analyses are certainly yet necessary, but despite of the fact that INT surely shows most of its effectiveness on schizophrenic onset, it should be considered and better assessed as an efficient rehabilitation tool also in chronic schizophrenic inpatients.

Conflict of interests: the authors have no conflict of interests to declare.

REFERENCES

1. Dauvermann M, Whalley H, Schmidt A, et al. Computational neuropsychiatry – schizophrenia as a cognitive brain network disorder. *Front Psychiatry* 2014; 5: 1-19.
2. Heinrichs RW, Zakzanis KK. Neurocognitive deficit in schizophrenia: a quantitative review of the evidence. *Neuropsychol Rev* 1998; 12: 426-45.
3. Ueland T, Rund BR. A controlled randomized treatment study: the effects of a cognitive remediation program on adolescents with early onset psychosis. *Acta Psychiatr Scand* 2004; 109: 70-4.
4. Rocca P, Galderisi S, Rossi A, et al. Disorganization and real-world functioning in schizophrenia: results from the multicenter study of the Italian Network for Research on Psychoses. *Schizophr Res* 2018; 210: 105-12.
5. Bucci P, Galderisi S, Mucci A, et al. Premorbid academic and social functioning in patients with schizophrenia and its associations with negative symptoms and cognition. *Acta Psychiatr Scand* 2018; 138: 253-66.
6. Merlotti E, Mucci A, Caputo F, Galderisi S. Cognitive deficits in psychotic disorders and their impact on social functioning. *J Psychopathol* 2018; 24: 42-7.
7. Bersani G, Iannitelli A. La legalizzazione della cannabis: tra irresponsabilità politica e deresponsabilizzazione degli psichiatri. *Riv Psichiatr* 2015; 50: 195-8.
8. Quartini A, Pacitti F, Bersani G, Iannitelli A. From adolescent neurogenesis to schizophrenia. Opportunities, challenges and promising interventions. *Biomed Rev* 2017; 28: 66-73.
9. Parnanzone S, Serrone D, Rossetti MC, et al. Alterations of cerebral white matter structure in psychosis and their clinical correlations: a systematic review of Diffusion Tensor Imaging studies. *Riv Psichiatr* 2017; 52: 49-66.
10. Ceccanti M, Iannitelli A, Fiore M. Italian Guidelines for the treatment of alcohol dependence. *Riv Psichiatr* 2018; 53: 105-6.
11. Mazza M, Pollice R, Pacitti F, et al. New evidence in theory of mind deficits in subjects with chronic schizophrenia and first episode: correlation with symptoms, neurocognition and social function. *Riv Psichiatr* 2012; 47: 327-36.
12. Hogarty C, Flesher S, Ulrich R, et al. Cognitive enhancement therapy for schizophrenia. *Arch Gen Psychiatry* 2004; 61: 866-76.
13. Paquin K, Wilson AL, Cellard C, Lecomte A, Potvin S. A systematic review on improving cognition in schizophrenia: which is the more commonly used type of training, practice or strategy learning? *BMC Psychiatry* 2014; 14: 139.
14. Horan PW, Green FM. Treatment of social cognition in schizophrenia: current status and future directions. *Schizophr Res* 2019; 203: 3-11.
15. Mazza M, Lucci G, Pacitti F, et al. Could schizophrenic subjects improve their social cognition abilities only with observation and imitation of social situations? *Neuropsychol Rehabil* 2010; 20: 675-703.
16. Fisher M, Herman A, Stephens DB, Vinogradov S. Neuroscience-informed computer-assisted cognitive training in schizophrenia. *Ann NY Acad Sci* 2016; 1366: 90-114.
17. Borriello A, Balbi A, Menichincheri RM, Mirabella F. Timing and effectiveness of Brenner's IPT cognitive training in early psychosis. A pilot stud. *Riv Psichiatr* 2015; 50: 127-33.
18. Grant N, Lawrence M, Preti A, Wykes T, Cella M. Social cognition interventions for people with schizophrenia: a systematic review focusing on methodological quality and intervention modality. *Clin Psychol Rev* 2017; 56: 55-64.
19. Mueller DR, Schmidt SJ, Roder V. Integrated psychological therapy: effectiveness in schizophrenia inpatient settings related to patients' age. *Am J Geriatr Psychiatry* 2013; 21: 231-41.
20. Vita A, Comazzi M (a cura di). INT- Terapia neurocognitiva integrata nel trattamento della schizofrenia. Milano: Springer, 2015.
21. Barlati S, Valsecchi P, Galluzzo A, et al. Implementing cognitive rehabilitation interventions for schizophrenia patients in mental health services: focus on Integrated Psychological Therapy (IPT). *J Psychopatol* 2018; 24: 79-87.
22. Fisher M, Herman A, Stephens DB, Vinogradov S. Neuroscience-informed computer-assisted cognitive training in schizophrenia. *Ann NY Acad Sci* 2016; 1366: 90-114.
23. Grynspan O, Perbal S, Pelissolo A, et al. 2011. Efficacy and specificity of computer-assisted cognitive remediation in schizophrenia: a meta-analytical study. *Psychol Med* 2011; 41: 163-73.
24. Zimmer M, Verissimo Duncan A, Laitano D, Ferreira EE, Belmonte-de-Abreu P. A twelve-week randomized controlled study of the cognitive-behavioral Integrated Psychological Therapy program: positive effect on the social functioning of schizophrenic patients. *Rev Bras Psiquiatr* 2007; 9: 140-7.
25. Jones M. Ideologia e pratica della psichiatria sociale. Milano: Etas, 1970.
26. American Psychiatric Association. Manuale Diagnostico e Statistico dei Disturbi Mentali DSM-5. Milano: Raffaello Cortina Editore, 2014.
27. Roeder V, Muller DR, Schmidt SJ. Effectiveness of Integrated psychological therapy (IPT) for schizophrenia patients: a reanalysis update. *Schizophr Bull* 2011; 37 Suppl 2: S71-9.
28. Randolph C. RBANS Repeatable Battery for the Assessment of Neuropsychological Status. Firenze: Giunti OS, 1998.
29. Nocentini U, Di Vincenzo S, Panella M, Pasqualetti P, Caltagiorno C. La valutazione delle funzioni esecutive nella pratica neuropsicologica: dal Modified Card Sorting Test al Modified Card Sorting Test – Roma Version. Dati di standardizzazione. *Nuova Rivista di Neurologia* 2002; 12 (1).
30. Cirillo MA, Siedman LJ. Verbal declarative memory dysfunction in schizophrenia: from clinical assessment to genetics and brain mechanisms. *Neuropsychol Rev* 2003; 13: 43-77.
31. Covington AJ, He C, Brown C, et al. Schizophrenia and the structure of language: the linguistic's view. *Schizophr Res* 2005; 77: 85-98.
32. Wrobel J. Language and schizophrenia. Amsterdam: J Benjamins Pub, 1990.

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33. Prentice K, Glod MJ, Buchanan RW. The Wisconsin Card sorting Test impairment in schizophrenia is evident in first four trials. *Schizophr Res* 2008; 106: 81-7.
34. Chiang-Shan Ray L. Do schizophrenia patients make more perseverative than non-perseverative errors on the Wisconsin Card Sorting test? A meta-analytic study. *Psychiatry Res* 2004; 129: 179-90.
35. Galderisi S, Rucci P, Kirkpatrick B, et al. Interplay among psychopathologic variables, personal resources, context-related factors, and real-life functioning in individuals with schizophrenia a network analysis. *JAMA Psychiatry* 2018; 75: 396-404.
36. Sampogna G, Fiorillo A, Luciano M, et al. A randomized controlled trial on the efficacy of a psychosocial behavioral intervention to improve the lifestyle of patients with severe mental disorders: study protocol. *Front Psychiatry* 2018; 9: 235.