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THE EFFECT OF ANTIPSYCHOTIC THERAPY ON SOCIAL INFERENCE AND EMOTION RECOGNITION IN SCHIZOPHRENIC PATIENTS

Abstract

Objectives: Social cognition is described as the mental operations underlying social interactions including the human ability and capacity to perceive intentions and dispositions of others and it is involved in functional outcomes. Pharmacological studies on this topic are few, therefore our goal is to compare the effect on social cognition and social inference of second, first-generation and long acting antipsychotics.

Materials and Methods: This work arises from the Italian Network Research on Psychosis (NIRP). From March 2012 to December 2015, 62 schizophrenic patients in stable psychopathological conditions were recruited. Each patient was tested with the Positive and Negative Syndrome Scale (PANSS), the Brief Negative Symptom Scale (BNSS), the Facial Emotion Identification Test (FEIT) and The Awareness of Social Inference Test (TASIT).

Results: Patients treated with atypical antipsychotics better recognize neutral expression at TASIT1 while patients treated with typical neuroleptics recognize a higher percentage of sadness at FEIT. Patients receiving long-acting therapy interpret better sincere remarks and paradoxical sarcasm at TASIT2 and have a higher percentage of correct answers at FEIT. Considering the entire sample, our study demonstrates a big impact of duration of the illness, independently from patients' age.

Conclusions: Our results highlight the need for further investigations about social cognition in schizophrenic patients in order to provide personalized and integrated programs and ameliorate clinical outcome of these patients.

Key words: social cognition, antipsychotic therapy, emotion recognition, social inference, schizophrenia

Introduction

Social cognition is described as the "mental operations underlying social interactions including the human ability and capacity to perceive intentions and dispositions of others" [1]. It is composed of five domains: theory of mind or mentalization, emotion recognition ability, attributional style, social knowledge and social perception or social inference [2].

Over the last decade, clinical investigators and behavioral scientists have increasingly employed social cognitive constructs to explore the symptoms and interpersonal deficits that characterize schizophrenia. Indeed, social cognition has emerged as a high priority topic within schizophrenia research as evidenced by a burgeoning empirical literature and increased attention in scientific meetings [2].

One of the most important aspects of social cognition is emotion perception. Deficits in this domain have been widely acknowledged in schizophrenic patients [3-6]. Social inference is another key domain of social cognition; it is related to community functioning, and should be

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a target for interventions designed to enhance functional improvements in schizophrenic patients [27]. Until now, this issue has been relatively understudied in schizophrenia, despite evidence of the relationship between functional outcome and social cognition [7]. Although social cognition has not been commonly used as an endpoint for intervention studies, it is increasingly viewed as a treatment target for both pharmacological and non-pharmacological (psychosocial) interventions [2]. Currently, there are only few studies about the impact of medication on social cognition, and particularly on emotion perception. Moreover, a recent review of the literature, concluded that antipsychotics were unlikely to facilitate the recovery of social cognition deficits in schizophrenia [8].

The most investigated aspect of social cognition is emotion processing. Similarly to the results described by Kucharska Pietura & Mortimer [8], a review about facial emotion recognition found that antipsychotic medication did not seem to successfully treat this aspect of schizophrenia [9]. The literature about this issue reports mixed results; anyway, treatment effects are likely small, or affected by moderating factors such as age, gender or type of medication. Kee and coworkers reported a benefit in emotion perception for risperidone compared to haloperidol in a small (N = 20) double-blind pilot study with random assignment to medication. In an open-label study without random assignment (N = 52) [10], Littrell and coworkers found a benefit for olanzapine compared with a variety of first-generation medications on a social perception measure [11]. No benefit was reported for risperidone on emotion perception in a small (N = 13) crossover study in patients with first-episode psychosis [12]. Similarly, Harvey and coworkers found that patients randomly assigned to risperidone (N = 142) or quetiapine (N = 124) did not improve on a lone measure of emotion perception over the 8-week study period [13].

Briefly, the studies to date have involved either small samples, single measures of social cognition, or non-randomized designs, not allowing for definitive conclusions about the influence of antipsychotic medications on social cognition or the relative benefit of first- versus second-generation medications. Duration of illness has been shown to be a marker of poor prognosis and has been associated with poorer outcome [14], but regrettably most of the studies do not assess the possible impact of this variable.

The current research aimed to add to the current dearth of studies about the impact of antipsychotics on social cognition and social inference, focusing on the possible differences between second and first-generation antipsychotics.

Materials and Methods

Data collection for this research started in the context of the Italian Network for Research on Psychoses [15], a multicenter, observational, case-control study. This study was conducted from March 2012 to September 2013 in 26 Italian University psychiatric clinics and/or mental health departments. For this study, our center recruited 44 schizophrenic patients among those treated by the Psychiatry institute (SC Psichiatria) of the University Hospital "Maggiore della Carità", Novara. To increase our sample size, we continued the recruitment even after the end of the national project, until December 2015, enrolling 18 patients more.

Inclusion criteria were: a diagnosis of schizophrenia according to DSM-IV-TR criteria; 18 to 66 years of age; patients in good/stable psychopathological conditions (no treatment modifications and /or hospitalization due to symptoms exacerbation in the three months preceding assessment).

Exclusion criteria were: a diagnosis of dementia or moderate to severe mental retardation, history of head trauma with loss of consciousness, symptoms due to alcohol/substance abuse in the last six months, neurological disorders, current pregnancy or lactation, insufficient knowledge of Italian language.

Written informed consent was obtained from each patients or their legal guardians. The research was approved by our local Ethical Committee (Protocollo 283/EC, studio n EC 43/12).

We collected data on age, sex, type of medication, duration of illness and education, using all available sources of information (patient, family members and caregivers, medical records). The Positive and Negative Syndrome Scale (PANSS) [16] was used to assess symptom severity; negative symptoms were rated using the Brief Negative Symptom Scale (BNSS) [17 18]. Patients were tested with the Facial Emotion Identification Test (FEIT) [19 20] and The Awareness of Social Inference Test (TASIT) to investigate the recognition of facial expression and the social cognition [21].

The TASIT is an audiovisual tool based on 59 brief clips played by professional actors, designed for the clinical assessment of social perception. It assesses emotion recognition and the ability to interpret conversational remarks which are meant literally (i.e., sincere remarks and lies) or non-literally (i.e., sarcasm) as well as the ability to make judgments about

the thoughts, intentions and feelings of speakers [21]. The FEIT consists of 55 black and white pictures of male and female adults, presented trough a computerized presentation, showing 7 different facial emotion: happiness, sadness, fear, anger, surprise, disgust, neutrality. The patient has hence to match each images with the appropriate facial emotion [19][20].

Descriptive statistics were performed using frequencies and percentages tables for categorical variables. Continuous variables were analyzed with ANOVA and post-hoc analyses (Tukey method), and non parametric tests were performed as well (SPSS 21).

Results and Conclusions

Our total sample included 62 patients: 11 patients treated with first generation antipsychotics, 40 patients treated with second generation antipsychotics and 11 patients with an association of the two classes of drugs. Furthermore, we divided the sample into two subgroups based on the method of administration of the therapy: 46 patients were treated only with oral medication, while 16 patients received long acting injectable therapy.

Patients treated with second generation antipsychotics better recognized neutral expression at TASIT1 compared to those treated with a combination of typical/atypical drugs (p < 0.05), while we found no difference with patients treated with first generation antipsychotics. Patients treated with first generation antipsychotics recognized a higher percentage of sad faces at FEIT than patients treated with atypical neuroleptics (p < 0.05). Our study is one of the first about the impact of antipsychotics on the recognition of a single emotions at FEIT, usually in fact, litera-

ture studies use as an endpoint the total percentage of correct answer at FEIT without focusing on single emotions; it is therefore difficult to compare our results with the existing literature.

As far as long acting therapy is concerned, statistical analyses found that patients receiving long-acting therapy better interpreted sincere remarks and paradoxical sarcasm at TASIT2 than subjects in treatment with oral therapy (p < 0.05). Patients in therapy with long acting drugs had a higher percentage of correct answers at FEIT compared with patients treated only with oral therapy (p < 0.05). Our result confirm literature data about the impact on social functioning of long acting antipsychotics compared to the oral ones. Unfortunately, treatment outcome studies focused on this topic have used social functioning total scores as an endpoint and they do not consider subscales targeting specific domains (e.g. social, residential, and vocational), it is therefore difficult to make comparison of single domains with our results [22].

Considering the whole sample, our study showed a significant impact of illness duration on social inference and emotion recognition, independently from patients' age: patients with a longer history of the disease performed worse at both FEIT and TASIT. (See Table I) Consistent with our results, literature's evidence correlate duration of illness with poor prognosis; moreover duration of illness seems to be related with treatment efficacy [14]. It would be interesting to correlate the performance on FEIT and TASIT with the duration of untreated psychosis (DUP), in the light of evidence that suggests that DUP has a significant impact on clinical and social outcome [23].

In conclusion, our results failed to find a major efficacy of second generation antipsychotics on social

Table I.

		Pearson Correlation	Sig. (2-tailed)
Duration of illness	TASIT 1 surprise	-.298	.019
	TASIT 1 neutrality	-.359	.013
	TASIT 1 disgust	-359	.013
	FEIT% CORR ANS	-.266	.037
	FEIT% anger	-.287	.024
	FEIT% disgust	-.268	.044
	FEIT% M faces	-.257	.044
	BNSS asociality	.256	.045
	BNSS blunted affect 9	.254	.046
	BNSS blunted affect 10	.292	.021
	BNSS blunted affect 11	.302	.017
	BNSS alogia	.257	.044

inference and emotion recognition [10] [11]. Anyway, as described above, the results about this issue are mixed, and some reviews found no benefit of second generation antipsychotics on emotion perception [12]. Briefly, literature results are heterogeneous, samples are frequently too small and the methods used are different, hindering the possibility to compare and generalize the results. Further investigations about social cognition in schizophrenic patients are warranted in order to allow the implementation of personalized and integrated treatment programs to improve the clinical outcome of schizophrenic patients.

References

[1] Brother L. *The social brain: a project for integrating primate behavior and neurophysiology in a new domain*. Concepts Neurosci 1990;1:27-61.

[2] Green MF, Penn DL, Bentall R, et al *Social Cognition in schizophrenia: an NIMH Workshop on Definitions, Assessment, and Research Opportunities.* Schizophr Bull 2008;34:1211-20.

[3] Edwards J, Jackson HJ, Pattison PE,. *Emotion recognition via facial expression and affective prosody in schizophrenia: a methodological review* Clin Psychol Rev 2002;22:789-832.

[4] Hellewell JSE, Whittaker JF, Mueser KT, et al. *Affect perception and social knowledge in schizophrenia.* In: Mueser KT, Tarrier N. Handbook of social functioning in schizophrenia. Allyn & Bacon 1998, pp. 197-212.

[5] Kohler CG, Brennan AR, *Recognition of facial emotions in schizophrenia.* Curr Opin Psychiatry 2004:17:81-6.

[6] Mandal MK, Pandey R, Prasad AB, *Facial expressions of emotions and schizophrenia: a review.* Schizophr Bull 1998;24:399-412.

[7] Couture SM, Penn DL, Roberts DL, *The functional significance of social cognition in schizophrenia: a review.* Schizophr Bull 2006;32:S44-S63.

[8] Kucharska-Pietura K, Mortimer A. *Can antipsychotics improve social cognition in patients with schizophrenia?* CNS Drugs 2014;27:335-43.

[9] Hempel RJ, Dekker JA, van Beveren NJM, et al. *The effect of antipsychotic medication on facial affect recognition in schizophrenia: a review*. Psychiatry Res 2010;178:1-9.

[10] Kee KS, Kern RS, Marshall BD, et al. *Risperidone versus haloperidol for perception of emotion in treatment-resistant schizophrenia: preliminary findings*. Schizophr Res 1998;31:159-65.

[11] Littrell KH, Petty RG, Hilligoss NM, et al. *Improvement in social cognition in patients with schizophrenia associated with treatment with olanzapine*. Schizophr Res 2003;66:201-2.

[12] Herbener ES, Hill SK, Marvin RW, et al. *Effects of antipsychotic treatment on emotion perception deficits in first-episode schizophrenia.* Am J Psychiatry 2005;162:1746-8.

[13] Harvey PD, Patterson TL, Potter LS, et al. *Improvement in social competence with short-term atypical antipsychotic treatment: a randomized, double-blind comparison of quetiapine versus risperidone for social competence, social cognition, and neuropsychological functioning.* Am J Psychiatry 2006;163:1918-25.

[14] Rapado-Castro M, Berk M, Venugopal K, et al. *Towards stage specific treatments: effects of duration of illness on therapeutic response to adjunctive treatment with N-acetyl cysteine in schizophrenia.* Prog Neuropsychopharmacol Biol Psychiatr 2015;3:69-75.

[15] Galderisi S, Rossi A, Rocca P, et al. *The influence of illness-related variables, personal resources and context-related factors on real-life functioning of people with schizophrenia*. World Psychiatry 2014;13:275-87.

[16] Kay SR, Fiszbein A, Opler LA. *The positive and negative syndrome scale (PANSS) for schizophrenia*. Schizophr Bull 1987;13:261-76.

[17] Mucci A, Galderisi S, Merlotti E, et al. *The Brief Negative Symptom Scale (BNSS): Independent validation in a large sample of Italian patients with schizophrenia*. Eur Psychiatry 2015;3:641-7.

[18] Kirkpatrick B, Strauss GP, Nguyen L, et al *The brief negative symptom scale: psychometric properties*. Schizophr Bull 2011;37:300-5.

[19] Ekman P, Friesen WV. *Pictures of facial affect*. San Francisco, CA: Human Interaction Laboratory, University of California Medical Center 1976.

[20] Kerr L, Neale JM. *Emotion perception in schizophrenia: specific deficit or further evidence of generalized poor performance?* J Abnorm Psychol 1993;102:312-8.

[21] McDonald S, Bornhofen C, Shum D, et al. *Reliability and validity of The Awareness of Social Inference Test (TASIT): a clinical test of social perception.* Disabil Rehabil 2006;28:1529-42.

[22] Koshikawa Y, Takekita Y, Kato M, et al. *The comparative effects of risperidone long-acting injection and paliperidone palmitate on social functioning in schizophrenia: a 6-month, open-label, randomized controlled pilot trial.* Neuropsychobiology 2016;73:35-42.

[23] Malla AK, Bodnar M, Joober R, et al. *Duration of untreated psychosis is associated with orbital-frontal grey matter volume reductions in first episode psychosis.* Schizophr Res 2011;125:13-20.