



Theory of mind and schizophrenia in young and middle-aged patients: Influence of executive functions



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ABSTRACT

Theory of Mind (ToM) is compromised in schizophrenia, and responsible for social disability. We aim to study the correlation between ToM deficits and Executive Functions (EF), using the Faux Pas Test (FPT) for ToM evaluation, Behavioral Assessment of the Dysexecutive Syndrome (BADS) and Wisconsin Card Sorting Test (WCST) for EF assessment. Two groups of patients with schizophrenia were included: 22 young (18–35 years-old) and 18 middle-aged (> 50 years-old) Patients, compared to age-matched Controls.

We found worst FPT performances in both groups of patients, but with a more generalized pattern of dysfunction in the middle-aged patient group. This group had worse EF scores than both controls and younger patients. The association of EF with FPT items was uneven. In young patients only empathy (Q6) remained significant after controlling for EF and level of education, while in middle-aged patients faux pas explanation (Q4), false belief (Q5) and total scores remained significant. In young patients only affective TOM was impaired. No correlation was found with clinical symptoms, nor age at onset of the disease.

We conclude that ToM deficit arises early during the course of the illness (already present in young patients), increases in middle-aged patients, and relates only partially with EF.

1. Introduction

Schizophrenia has a heterogeneous clinical presentation, cognitive impairment being one of its symptom dimensions. As Ayesa-Arriola et al. (2016), Fett et al. (2011) and Reichenberg (2010) described, cognitive impairments include deficits in working memory, EF, attention, processing speed and social cognition. The latter is a multi-dimensional construct comprising emotional processing, social perception and knowledge, attribution bias and theory of mind (ToM), defined as the ability to understand that others also have minds, with different and separate mental states from our own (Green et al., 2005). ToM has been shown to be compromised in schizophrenia (Altamura et al., 2015), relating to disorganized symptoms, paranoid delusions and severe positive and negative symptoms (Harrington et al., 2005; Mancuso et al., 2011; Ventura et al., 2010; Martinez et al., 2017). It has

been viewed as an important factor in predicting social disability (Brüne et al., 2007). One of the tasks evaluating ToM is the FPT (Baron-Cohen et al., 1999). This task taps the understanding of multiple mental states such as intentions, emotions and beliefs, in everyday social situations (Bottiroli et al., 2016). Understanding a faux pas requires to infer a representation of both the cognitive state of the character making a faux pas, and of the emotional states when the character receives a faux pas (Baron-Cohen et al., 1999). Hence, the FPT allows the assessment of both cognitive and affective components of ToM.

Executive functioning (EF) occupies a central role in neuropsychological theories of behavior control. If in some studies (Pickup, 2008; Woodward et al., 2009) ToM and EF have been reported as independent modules, in others (Champagne-Lavau et al., 2012; Langdon and Coltheart, 2001) impairment in ToM has been linked to EF.

Executive functions include control functions related to the

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inhibition of prepotent responses, shifting mental sets, monitoring performance, updating task demands, goal maintenance, planning, working memory, and cognitive flexibility, among others. To assess EF, one of the widely used test in schizophrenia is the Wisconsin Card Sorting Test (WCST) (Grant and Berg, 1948). It evaluates the ability to shift cognitive set through abstract reasoning in working memory (Miyake et al., 2000). Verbal fluency is also a verbal measure of EF. Both WCST and Verbal fluency have been found to be correlated with tasks assessing ToM such as the FPT in schizophrenia (Scherzer et al., 2015). However, ecological EF tests, as they were more related to outcome measures (Chaytor and Schmitter-Edgecombe, 2003) might have superior validity than traditional neuropsychological EF tests. Among them, the Behavioral Assessment of Dysexecutive Syndrome (BADs, Wilson et al., 1996) has been consistently used to assess executive deficits in schizophrenia (Krabbendam et al., 1999), as well as in elderly healthy subjects (Allain et al., 2005). Verbal fluency, problem solving, inhibition, working memory and cognitive flexibility, among others, influence ToM tasks (Bottiroli et al., 2016).

As EF decline more significantly in patients with schizophrenia than in normal ageing (Fucetola et al., 2000), it would also be expected that the impairment in ToM should be greater in older schizophrenic patients. In healthy subjects, ToM seems to be affected by ageing in both affective and cognitive dimensions (Duval et al., 2011), although conflicting studies state that ageing only impacts cognitive and not affective ToM (Shamay-Tsoory et al., 2007). FPT has proven sensitive to individual differences and age-related changes in ToM (Wang and Su, 2013). Using the FPT, Bottiroli et al. (2016) compared three age healthy subjects, one young, one young-old and one old-old adults assessing cognitive and affective aspects of ToM. They found that young adults outperform both young-old and old-old adults on cognitive ToM but not on affective ToM. Moreover the effect of age in cognitive ToM was mediated by the working memory updating ability.

To our knowledge only one study has looked into ToM in schizophrenia after 50 years old (Smeets-Janssen et al., 2013), without making the comparison with a younger patients' group.

In the present study, we intended to evaluate ToM and EF in a group of patients with Schizophrenia between 18 and 35 years old and a group over 50 years old compared to age-matched controls, with the hypotheses that in these two domains,

- young patients should be different than young controls, and middle-aged patients should be different than middle-aged controls, with lower performances in patients.
- EF could have an impact on TOM abilities in patients and controls.
- that an effect of age should exist within the patient groups
- lastly, to show different impairment in cognitive or affective TOM in patients with schizophrenia compared to aged-matched controls, with different profiles in the older group of patients compared to the younger group.

2. Materials and methods

2.1. Sample

Fifty participants with schizophrenia, all outpatients were recruited in the Research Center of Sainte Anne Hospital. Patients mainly come from the same catchment area in Paris (15th arrondissement), and for some of them and for controls, from the University department of our Research unit. Among them, 25 patients were aged between 18 and 35 years old (Young Patients) and 25 patients were aged over 50 years old (Middle-aged Patients). Inclusion criteria were age within the range of the study, clinical stability for at least 3 months, and the same anti-psychotic treatment for the previous 3 weeks. We recruited healthy age-matched controls (who were paid for their participation), 25 aged from 18 to 35 years old (Young Controls) and 25 aged more than 50 years old (Middle-aged Controls) from advertising and telephone

contacts. Exclusion criteria for controls were past or present psychiatric or neurological disorder and psychiatric disorder in first or second-degree relatives. Inclusion criteria for all participants were Mini Mental State Examination (Folstein et al., 1975) superior to 25/30 and at least ten years of education. Exclusion criteria for all participants were neurological or any other major medical condition, substance dependence criteria in the last twelve-month period, verbal IQ < 70 as evaluated using the National Adult Reading Test (NART-Nelson, 1982), sensorial deficit compromising vision, audition or communication and difficulties in comprehension or expression in the French Language.

On the course of the study, 14 participants have been excluded: seven Middle-aged Patients and one Young Patient, due to low scores in the FPT french version (36) control questions and two Young controls, one for a noticeable attention deficit and another for very low scores whatever the test. To perfectly match patients and controls for age (mean and range), we also excluded two Young Patients and two Middle-aged Controls.

The study received approval from our local ethics committee (CPP Cochin, Ile de France III, No. A01-02946). All subjects provided informed and written consent.

2.2. Clinical and neuropsychological evaluations

For the patient samples, we evaluated age at onset and duration of illness, number of episodes, current psychiatric treatment and symptom severity (using Positive and Negative Syndrome Scale, PANSS, Kay et al., 1987). Subjects were screened with the diagnostic interview for genetic studies (DIGS 3.0-Nurnberger et al., 1994) to attest the diagnosis and to exclude any comorbidity in patients, and to exclude psychiatric or neurological disease in controls.

2.2.1. Faux-Pas task

FPT presents 20 social scenarios (10 containing a *faux pas*), read out loud by the interviewer, with a printed copy handled to every participant (minimizing memory demands). Participants were asked “Did anyone say something they shouldn’t have said or something awkward?” (Q1). If a *faux-pas* was detected, five other questions were asked: “identify the character who has committed the *faux-pas*” (Q2), “identify the content of the *faux-pas*” (Q3), “find an explanation for the *faux-pas*” (Q4), “assess the understanding of the character’s false-belief” (Q5) and “describe the character’s feelings” (Q6). The cognitive ToM component was assessed with the item “find an explanation for the *faux-pas*” (Q4), and “understanding of the character’s false-belief” (Q5), and the affective ToM component was assessed “with the description of the character’s feelings” (Q6). For all scenarios, two control questions unrelated to *faux-pas* were asked to evaluate the scenario’s factual comprehension. One point was given for each question concerning scenarios with a *faux-pas* (total of six points), two points if the participants correctly rejected the existence of a *faux-pas*. We attributed individual scores for scenarios containing a *faux-pas* (sub-scores for the different items and total score) and scenarios without a *faux pas* (total score). Control score included performance on control questions for all 20 scenarios.

2.2.2. Executive function assessment

EF assessment included the Battery of Assessment of Dysexecutive Syndrome (BADs), which contains 6 sub-tests: rule shift cards, action program, key search, temporal judgement, zoo map and modified six elements test, each one with a 4-point score (max = 24). We also used the Wisconsin Card Sorting Test (WCST) for cognitive flexibility, taking into account the number of categories achieved, number of total errors and number of perseverative errors. Verbal Fluency test was applied to assess semantic memory, implied in FPT. Global efficiency (IQ) was assessed through the NART.

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