Cognitive control and schizophrenia: The greatest reliability of the Stroop task

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ABSTRACT

Three components of cognitive inhibition were compared in patients with schizophrenia and healthy controls. Nineteen patients with schizophrenia were compared to 30 healthy controls, matched for age, sex, and educational level. Cognitive inhibition was examined by (i) access to relevant information (Reading with distraction task), (ii) suppression of no longer relevant information (Trail Making Test B), and (iii) restraint of cognitive resources to relevant information (Stroop Test, Hayling Sentence Completion Test, Go/No-Go Test). Beck Depression Inventory, and Positive and Negative Syndrome Scale were also used. Compared to healthy controls, patients with schizophrenia and stabilized for at least 6 months were slower in the inhibition condition at the Stroop task, read more distractors at the RWD, and made more perseverative errors at the TMT, even after controlling for age, Mini-Mental State Examination score, information speed processing, and accuracy. This difference remained significant after taking into account the level of depressive symptoms and the severity of psychotic symptoms. In multivariate analyses, only the Stroop interference index explained cognitive inhibition deficit in patients with schizophrenia. The abnormal cognitive inhibition process observed in patients with schizophrenia could therefore concerns the ability to restraint, rather than the access or the suppression processes.

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1. Introduction

It is becoming increasingly clear that schizophrenia is characterized by heterogeneous brain abnormalities involving cerebral regions involved in executive functions (Raffard and Bayard, 2012). Executive control, usually enabling to flexibly adapt behavior to meet current demands (Barch et al., 2009), is one of the most clearly impaired cognitive features of schizophrenia, especially in the face of ambiguous, complex and or changing environments (Botvinick et al., 2001). Thus, cognitive control impairment has been hypothesized to also reduce one's ability to respond adaptively to stressors. Executive control is a general ability that underlies performance on different types of tests, including those assessing task switching, cognitive inhibition, error detection, response conflict and cognitive flexibility (Miller and Cohen, 2001). Regarding clinical impact, a deficit in executive control in schizophrenia was associated with social isolation, poor interpersonal relationships (Bozikas et al., 2006), reduced quality of life (Addington and Addington, 2000), and low self-esteem (Wang et al., 2013a).

Cognitive inhibition, a major component of executive control which is required for active suppression, limiting the processing of irrelevant stimuli for an on-going task (Shallice and Burgess, 1991), may be deficient in schizophrenia. Several studies have reported impaired inhibitory control in schizophrenia (Enticott et al., 2008; Kiehl et al., 2000;Raemaekers et al., 2002; Tan and Rossell, 2014; Wang et al., 2013b; Zandbelt et al., 2011), but others have not (Badcock et al., 2002; Nishimura et al., 2011; Rubia et al., 2001). This may be due to the fact that cognitive inhibition is probably a heterogeneous concept (Hasher et al., 1999), the latter studies having used a variety of tasks measuring different aspects of inhibition (Aron, 2007). According to Hasher and Zacks (Hasher et al., 1999), inhibitory mechanisms indeed serve to (i) restrict access to relevant information, (ii) suppress information that is no longer relevant, and (iii) restrain production of strong but potentially incorrect retrieval of

information from working memory (Zacks et al., 1999). Furthermore, only one pilot study (Gigaux et al., 2013) explored the Hasher and Zacks' paradigm of cognitive inhibition (Hasher et al., 1999) in schizophrenia. Since most of the studies were behavioral, the neural mechanisms underlying impaired inhibitory control in schizophrenia remain largely unknown. Nevertheless, it is not clear to what extent cognitive inhibition deficits are heterogeneous in schizophrenia patients. Furthermore, it has been shown that attention and executive function (including response inhibition) predicted level of global functioning (Hegde et al., 2013). Multiple studies have demonstrated that cognitive control impairments in schizophrenia are largely mediated by slowed information processing speed (Hegde et al., 2013).

Apart from understanding more clearly the types of cognitive deficits associated with schizophrenia, research works devoted to inhibition deficits could provide which aspect of cognitive inhibition is driving most of its abnormality when taking into account numerous intermediate markers of schizophrenia, potentially offering targets of therapeutic interventions aimed at adapting the long-term management of care.

The aim of this study was to verify the abnormality of cognitive inhibition ability in patients with schizophrenia during the stabilization phase of their disease compared to healthy controls, in order to disentangle which component of cognitive inhibition is the most specifically impaired, even when potential confounders are taken into account. We hypothesized that patients with schizophrenia would show a significant deficit in cognitive inhibition, and that the three aspects of inhibition process (access, suppression and restraint) would be heterogeneously impaired. Impact of poor inhibition may explain high levels of co-morbid substance abuse associated with the disorder (Chambers et al., 2001), violent offending in patients suffering from schizophrenia (Enticott et al., 2008), a predisposition to hallucinations (Paulik et al., 2008) and frequency of hallucinations in schizophrenic patients (Waters et al., 2003), and may also predict poor occupational and social outcome (Reeder et al., 2004). The level of cognitive functioning has been shown to be an important predictor for recovery and functional outcome (Harvey et al., 1998; Kurtz et al., 2008), underlining the importance of achieving a better understanding of the nature of cognitive deficits associated with schizophrenia in order to optimize rehabilitation and intervention programs. Indeed, cognitive remediation could be adapted to focus more precisely on these cognitive functions in order to improve or avoid the decrease of such cognitive skills.

2. Method

2.1. Population

Two groups of participants aged between 21 and 65 years were recruited: 1) 19 outpatients with schizophrenia (paranoid type) during the stabilization phase of their disease (as assessed by DSM-IV-TR criteria), and 2) 30 healthy controls with no lifetime personal history of psychiatric disorders. To reduce heterogeneity of executive functions according the subtype of schizophrenia (Brazo et al., 2002), only outpatients with paranoid subtype of schizophrenia were recruited.

Patients and controls were all French natives, with a Mini-Mental State Examination score ≥ 25 (21). Written informed consent was obtained from all participants. The study was conducted in accordance with the ethical standards set forth in the Helsinki Declaration (1983). The local ethics committee approved the project.

Lifetime axis I psychiatric diagnoses were made according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) with the MINI by two experienced psychiatrists (S.R.D. and M.O.). During the same period, healthy controls without any psychiatric or neurological history, and no psychotropic medication were recruited by advertisement in the community. Non-inclusion criteria for both groups were bipolar disorder, affective disorders, electroconvulsive therapy in the previous 6 months, neurological disorders (stroke, epilepsy, and brain tumor or injury), and intellectual disability.

Outpatients with schizophrenia (mean age=41.6 [30–63] years, 47.4% of female) were comparable to healthy controls (mean age=42.3 [21–65] years; 30% of female) for age, educational level, and MMSE score ≥ 25. All patients were recruited during the stabilization phase of their disease, with no hospitalization, relapse, and no medication changes within the previous 6 months of the day of the inclusion. All patients received a comparable dosage of antipsychotics (equivalent of 200 mg of chlorpromazine). Beck Depression Inventory for depression, and Positive and Negative Syndrome Scale (PANSS) for psychotic symptoms were used.

2.2. Neuropsychological assessments

The three domains of cognitive inhibition were evaluated on the basis of Hasher and Zacks' theoretical model (Hasher et al., 1999): 1) *access* with the "Reading with distraction task" (RWD) (Connelly et al., 1991), 2) *suppression* with the Trail Making Test (TMT) (Godefroy et al., 2008), and 3) *restraint* with the traditional card version of Stroop Color Test (Godefroy et al., 2008), the Hayling Sentence Completion Test (HSC) (Burgess and Shallice, 1996). Besides, motor inhibition was measured by the Go/No-Go Test (Godefroy et al., 2008).

Reading-With-Distraction task (Connelly et al., 1991), participants are asked to read four different stories. There are four forms for each story: the first form is the original story (T1), printed in a standard font. The other forms are similar to the initial version with the exception of additional distracting words printed in italic. Three types of distracting words are included: semantically related distracting words in the second form (T2), neutral distracting words in the third form (T3) and non words in the fourth form (T4). All of the distracting words are emotionally neutral. Before beginning the task, participants are asked to read clearly the original form of the story and are informed that in the other versions, the text is printed in standard and italic fonts, including distracting words; they are asked to read only the original version and ignore the distracting words.

In the first part of the Stroop Test, participants are asked to read words printed in black, all words naming colors. In the second part, the same words are printed in color and participants are asked to give the color of the ink; the name of the color corresponding to that of the word describing this color. In the third part, subjects are asked to name the color of the ink, which does not correspond to the word they are reading (e.g. the word "green" printed in blue).

In the Trail Making Test, the participants are asked to connect circles as quickly as possible, without lifting the pencil from the paper. Twenty-five circles are distributed over a sheet of paper. In Part A, the circles are numbered 1–25, and the participant must draw lines to connect the numbers in ascending order. In Part B, the circles include both numbers (1–13) and letters (A–L). Participants are asked to draw lines to connect the circles by alternating between the numbers and letters in ascending order (i.e., 1-A-2-B-3-C, etc.).

The Hayling Sentence Completion test consists of 30 sentences in which the final word is omitted but is highly predictable in everyday language situations. The task is made up of two sections (A and B), each one containing 15 sentences. In section A (response initiation), the sentences are read aloud to the individual, who has to complete each one with the missing word as quickly as possible. For example, in the sentence "He posted a letter forgetting to put on a…," the correct response should be "stamp." In section B (response inhibition), the sentences are read aloud to the subject, who is asked to complete each one with an unexpected word that is absolutely unrelated to the sentence presented, as quickly as possible. For example, for the sentence "The farmer went to milk the…," participants might give the word "phone." During this inhibition section, participants who completed the sentence with a related word rather than an unrelated one are told that their word is related to the sentence, and ask to follow the task instructions, which are then repeated. If the participant does not produce a word within 30 s, the trial is terminated and a response latency of 30 s is recorded.

All neuropsychological testing was conducted in one session (in a random order) at the same time of the day (between 2:00 and 4:00 p.m.) by an evaluator blind to clinical ratings and schizophrenia history.

2.3. Statistical analyses

Comparisons of quantitative values between groups were performed using a T-test. A Chi-square test was used to compare qualitative values. The correlation between two quantitative variables was estimated by the Pearson correlation coefficient.

Second, uni and multiple linear regression analyses were performed to specify the associations between schizophrenia (dependent variable) and neuropsychological tests scores (independent variable). Separated analyses were performed for each inhibition test score, adjusting for age, MMSE score, severity of depression, information processing speed of each task (measured by part 1 of the RWD total time to completion, TMT A total time to completion, Hayling part A total time to completion, Naming Stroop total time to completion), and accuracy of each task (measured by RWD Words read, TMT B Perseverations, Hayling B penalities, Inhibition Stroop uncorrected errors). Thus, information processing speed is an important variable to be taken into account when assessing inhibition impairments in patients with schizophrenia.

Finally, as the error distributions were zero-inflated, we used a generalized linear model with a negative binomial log link (which afforded the best fit for the distribution) to examine errors measured by each task, after checking that all included variables had a normal distribution. SPSS 21.0 (SPSS, Chicago, Illinois) was used to analyze the data.