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## Visual expertise for print in schizophrenia: Analysis of the N170 component

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#### ABSTRACT

Reading deficits have been reported for patients suffering from schizophrenia namely, specific phonological processing deficits. Phonological processing skills are crucial in the learning-to-read process as they are necessary to develop visual expertise for print, which reflects the neural specialization for print. The present study is the first to test visual expertise for print in patients suffering from schizophrenia by measuring the N170 component. Patients and pair-matched healthy control participants performed a lexical decision task, in which words and symbols were presented. As expected, larger N170 amplitudes to word than to control stimuli were observed at the left occipito-temporal site PO7 but not at the PO8. More importantly, the modulation of the N170 as a function of the stimulus and hemisphere did not vary between patients and controls. This result suggests preserved visual expertise for print processing in patients suffering from schizophrenia.

#### 1. Introduction

Schizophrenia is a psychiatric disorder characterized by clinical positive symptoms such as hallucinations and delusions, negative symptoms such as apathy and reduced expression of emotions, and disorganization of thought. Several cognitive disorders have been associated with schizophrenia, such as visual processing (Silverstein and Keane, 2011), time perception (Gómez et al., 2014), sustained attention (Hoonakker et al., 2017) and memory (Kraguljac et al., 2013; Wang et al., 2017). More recently, increasing evidence for a deficit in reading ability has emerged (Javitt and Sweet, 2015; Revheim et al., 2006; Revheim et al., 2014; Whitford et al., 2013; Whitford et al., 2018 for a review). This is of great concern as a good reading level is necessary in our modern society, be it in a professional environment, health related tasks (e.g. prescriptions), or societal and familial roles. Furthermore, cognitive remediation programs aimed at improving cognitive functions often use written material. Therefore, a good reading level is essential to be able to benefit from cognitive therapies.

Some studies have explored reading comprehension and word recognition in patients with schizophrenia. Standardized tests such as the Gray Oral Reading Test (GORT-4; Wiederholt and Bryant, 2001) and the Reading Comprehension Battery for Aphasia (RCBA; Lapointe and Horner, 1998) showed that patients suffering from schizophrenia had lower reading comprehension skills than controls (Arnott et al., 2011;

Carrion et al., 2015; Collins et al., 2014; Hayes and O'Grady, 2003; Revheim et al., 2006; Whitford et al., 2013). Some, but not all, studies on reading skills of patients suffering from schizophrenia observed less efficient automatic word recognition, as patients had lower single word decoding skills (Collins et al., 2014; Martinez et al., 2012), reading fluency and accuracy skills than controls (Arnott et al., 2011; Carrion et al., 2015; Hayes and O'Grady, 2003; Martinez et al., 2012; Revheim et al., 2006; Revheim et al., 2014; Whitford et al., 2013). These reading deficits already appeared at a young age before the symptomatic onset of the disease (Ambelas, 1992; Carrion et al., 2015; Fuller et al., 2002; Reichenberg et al., 2002) and may thus point to a developmental reading disorder.

In addition to a lower reading level, specific phonological processing deficits have been observed in patients suffering from schizophrenia (Arnott et al., 2011; Revheim et al., 2006; Revheim et al., 2014; Whitford et al., 2013). Patients obtained lower composite scores than controls in the subtests: phonological awareness (sound structure of a word), phonological memory (coding and storing of phonological information) and rapid naming (rapid retrieval of phonological information) in the Comprehensive Test of Phonological Processing (CTOPP; Wagner et al., 1999). According to the phonological mapping model, phonological processing skills are crucial in the learning-to-read process as they are necessary to develop visual expertise for print (McCandliss and Noble, 2003). Visual expertise for print reflects the

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 Table 1

 Demographic and clinical characteristics of the participants.

|                                    | Patients suffering from schizophrenia | Control subjects |                        |
|------------------------------------|---------------------------------------|------------------|------------------------|
|                                    | Mean (Std. err.)                      | Mean (Std. err.) |                        |
| Gender (male:female ratio)         | 13:9                                  | 13:9             |                        |
| Age (years)                        | 41.1 (8.8)                            | 40.3 (8.4)       | t(42) = -0.28, p = .78 |
| Education (years)                  | 12.3 (2.8)                            | 12.5 (2.7)       | t(42) = -0.27, p = .79 |
| Reading speed <sup>1</sup>         | 8.84 (1.82)                           | 9.26 (1.68)      | t(41) = -0.78, p = .43 |
| Reading efficiency <sup>2</sup>    | 417.4 (86.0)                          | 437.4 (82.2)     | t(41) = -0.77, p = .44 |
| Reading accuracy <sup>3</sup>      | 262.28 (2.24)                         | 262.09 (3.02)    | t(41) = 0.24, p = .81  |
| WAIS standard score                | 8.3 (2.4)                             | 9.7 (2.2)        | t(42) = -2.12, p = .04 |
| PMR percentile                     | 60.8 (30.5)                           | 77.6 (18.3)      | t(42) = -2.21, p = .03 |
| Antipsychotic dosage               |                                       |                  |                        |
| Chlorpromazine equivalent (mg/day) | 261 (144)                             | n.a.             |                        |
| Illness duration (years)           | 13.7 (7.4)                            | n.a.             |                        |
| PANSS score                        |                                       | n.a.             |                        |
| Total                              | 65.3 (15.6)                           |                  |                        |
| Positive                           | 15.3 (4.2)                            |                  |                        |
| Negative                           | 18.9 (6.3)                            |                  |                        |
| Disorganization                    | 7.4 (3.0)                             |                  |                        |
| Global                             | 31.1 (8.1)                            |                  |                        |

<sup>&</sup>lt;sup>1</sup>(1/reading time) \* 1000. <sup>2</sup>(number of words correctly read \* 180)/reading time. <sup>3</sup>number of words correctly read. WAIS: Wechsler adult intelligence scale, PMR: progressive matrices of Raven, PANSS: positive and negative syndrome scale.

neural specialization for print processing and emerges over the first years of reading acquisition through the acquisition of letter-sound associations (Maurer and McCandliss, 2008). The efficiency of the neural specialization is observed in early visuo-orthographic processing, around the N170 peak in left occipito-temporal regions (recorded at site PO7: Dien, 2009). This component has been associated with the activity of the left fusiform gyrus, more precisely with the visual word form area (Cohen et al., 2000). In typical readers, presentation of orthographic stimuli (i.e. words or letter strings) elicits larger N170 amplitude than non-orthographic stimuli (i.e. symbols) (Bentin et al., 1999). It is worth noting that dyslexic participants did not present such a modulation of N170 as a function of stimulus (Mahé et al., 2012). This absence of modulation does not result from a poor reading level as the classical effect of N170 (i.e., a greater N170 amplitude for words than symbols) is preserved for poor readers (i.e., healthy participants matched to dyslexics in reading level) (Mahé et al., 2013). In patients suffering from schizophrenia, activity of the visual word form area has been observed during word recognition in functional magnetic resonance imaging (fMRI) studies, by comparing patients and healthy controls (Li et al., 2007; Natsubori et al., 2014; Vinckier et al., 2014; Martinez et al., 2012). Results of these investigations are, however, inconsistent: either an increase was reported in activity of the visual word form area during word recognition for patients compared to control participants (Martinez et al., 2012), or a decrease in activity (Li et al., 2007), or no difference between patients and controls (Natsubori et al., 2014; Vinckier et al., 2014). Due to these inconsistent findings, it remains an open question as to whether the integrity of the visual word form in patients suffering from schizophrenia is intact. Using the electroencephalography (EEG) technique, with a much higher temporal resolution than fMRI, most of the studies with patients focused on the event-related potential (ERP) component N400 (Condray et al., 2010; Kostova et al., 2005; Salisbury, 2010a, 2010b). The N400 is a late negativity observed in the 300-600 ms post-stimulus-onset window and is linked to post-lexical semantic processes. When a semantic priming task was used with word pairs varying in lexical frequency (rare prime and target vs. frequent prime and target), an effect of lexical frequency was observed on the N400 component with a larger N400 amplitude for frequent pairs than for rare pairs in healthy control participants. However, in patients suffering from schizophrenia, this modulation of the N400 component as a function of lexical frequency was absent, indicating a deficit in accessing lexical representations (Condray et al., 2010).

Whereas several studies with patients focused on late ERP effects during the time course of word recognition, knowledge on neurocognitive process efficiency during the earlier steps of visual word processing is still limited. The neural specialization for print processing in patients with schizophrenia remains an issue to be addressed. Understanding the neural mechanisms underlying word recognition is crucial as they contribute to reading achievement. The present study explored the electrophysiological correlate of visual expertise for print in patients suffering from schizophrenia compared to control participants by investigating the N170 component. To this end, participants performed a lexical decision task (is the presented stimulus a word or not?) in which words and symbol strings were presented while recording EEG data.

#### 2. Methods and materials

#### 2.1. Participants

22 patients diagnosed with schizophrenia (mean ± standard error; 41.0 years ± 8.84 years) according to the Diagnostic and Statistical Manual of Mental Disorders TR-IV (DSM-4-TR, 2000) were recruited at Strasbourg psychiatric university hospital to participate in the present study. Patients were clinically stable and their medication had not been changed for at least three weeks prior to testing. Patients received average chlorpromazine equivalent doses of neuroleptics of 261 mg/ day  $\pm$  144 mg/day and the average duration of illness was of  $13.7 \, \text{years} \, \pm \, 7.4 \, \text{years}$ . The positive and negative syndrome scale (PANSS; Kay et al., 1987) was used to determine the current symptoms (total score 65.3  $\pm$  15.6, positive score 15.3  $\pm$  4.2, negative score  $18.9 \pm 6.3$ , disorganization score (Lepine disorganization score: sum of items P2, N5, G10 and G11; van Assche and Giersch, 2011) 7.4  $\pm$  3.0, global score 31.1  $\pm$  8.1). 22 pair-matched healthy control subjects (mean age 40.3 years  $\pm$  8.4 years) were included in the study. They matched patients suffering from schizophrenia in age, gender and education level (Table 1). All the participants were native French and right handed (handedness was self-reported). The exclusion criteria were dyslexia, neurological impairment, cranial trauma, general anesthesia, or the use of benzodiazepines or substance abuse in the three months prior to testing. The study was conducted in accordance with the Helsinki Declaration, all participants gave their written informed consent and the study procedure was approved by the Ethics Committee (CPP EST IV in Strasbourg, France).

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