



# Association of metabolic syndrome with sensory gating deficits in patients with chronic schizophrenia



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Received 8 January 2015; received in revised form 28 March 2015; accepted 6 April 2015

## KEYWORDS

Metabolic syndrome;  
Cognitive  
functioning;  
Sensory gating;  
P50 suppression;  
Schizophrenia

**Abstract** Metabolic syndrome is more prevalent in schizophrenia than in the general population and is associated with an increased rate of morbidity. It has been associated with cognitive impairments in schizophrenia, which are a core deficit in patients with chronic schizophrenia. Sensory gating deficit is also a core deficit in schizophrenia. The principal objective of this study was to investigate the relationship between sensory gating deficit and metabolic syndrome in patients with schizophrenia, after adjusting for key confounding factors. We hypothesized that patients with metabolic syndrome exhibit a higher rate of sensory gating deficit compared to those without metabolic syndrome. This study investigated sensory gating with the auditory event-related potential method by measuring P50 amplitude changes in a double click conditioning-testing procedure in 51 patients with schizophrenia. Patients with metabolic syndrome ( $n = 14$ ) had a higher rate of sensory gating deficit (P50 suppression

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<50%) ( $p < 0.001$ ) compared to those without metabolic syndrome ( $n = 37$ ). This result remained significant ( $B = 2.94$ ,  $Wald = 8.32$ ,  $p = 0.004$ ) after taking into account 5 potential confounding factors (age, gender, duration of disorder, Fagerström test, presence of clozapine or olanzapine). In patients without metabolic syndrome, sensory gating deficit was linked to a poorer attentional performance ( $\rho = -0.371$ ,  $p = 0.05$ ). In patients with metabolic syndrome, sensory gating deficit was linked to poorer memory performance ( $\rho = -0.635$ ,  $p = 0.02$ ). These findings suggest that metabolic syndrome may be linked to sensory gating deficit in patients with schizophrenia and that the relationship between neurocognitive function and sensory gating deficit could be affected by the metabolic status of the patients. Further studies are needed to address the causal relationship between sensory gating deficit related to schizophrenia, cognitive impairments and metabolic syndrome.

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## 1. Introduction

Cognitive impairments in memory, attention and executive functions (Nuechterlein et al., 2004) are critical determinants of functional disability in schizophrenia (Dickinson et al., 2004; Heinrichs and Zakzanis, 1998). Recently, emphasis has been placed on sensory and perceptual impairments, which are also critical in schizophrenia (Nelson et al., 2014; Postmes et al., 2014), and several types of sensory remediation have been proposed (Adcock et al., 2009; Fisher et al., 2009). Sensory gating deficit is considered to be a core perceptual deficit in patients with schizophrenic disorder (Javitt and Freedman, 2014). It can be assessed neurophysiologically using auditory event-related potential (ERP) methods by measuring P50 amplitude changes in double-click conditioning-testing procedures (Freedman et al., 1987). Healthy subjects have a >50% reduction in P50 amplitude after the second click (testing click). A reduction <50% indicates a sensory gating deficit (Freedman et al., 1983). This neurophysiological deficit has been associated with abnormal perceptual experience (Micoulaud-Franchi et al., 2014), which, like cognitive impairments, has been linked to functional disabilities in schizophrenia (Hetrick et al., 2012; Light and Braff, 2003).

Metabolic syndrome is more prevalent in schizophrenia than in the general population, with an overall rate ranging from 30% to 35% (Mitchell et al., 2013). Antipsychotic medications increase the risk of metabolic syndrome, in particular clozapine and olanzapine (Young et al., 2015). Metabolic syndrome is associated with an increased rate of morbidity and mortality (Goff et al., 2005). This increased rate of morbidity is related to an increased risk of cardiovascular disease and diabetes as well as an increased risk of functional disability (Medeiros-Ferreira et al., 2013), specifically via the effect of metabolic syndrome on cognitive impairment (Boyer et al., 2013; Friedman et al., 2012; Lancon et al., 2012; Li et al., 2014; Lindenmayer et al., 2012). Indeed, patients with metabolic syndrome perform significantly worse than patients without metabolic syndrome on tests of attention, memory and executive function (Boyer et al., 2013; Lancon et al., 2012; Li et al., 2014; Lindenmayer et al., 2012) and exhibit significant brain functional abnormalities related to these cognitive impairments (Boyer et al., 2014). This relationship does not seem to be confounded with the effect of antipsychotic medications (Boyer et al., 2013; Lancon et al., 2012; Li et al.,

2014; Lindenmayer et al., 2012). Metabolic changes may induce micro- and macro-cerebrovascular alterations, which might underlie impaired neural transmission and result in cognitive impairments (Lopresti and Drummond, 2013; Ramos-Rodriguez et al., 2013).

Sensory gating deficit has been related to cognitive impairments in patients with schizophrenia (Cullum et al., 1993; Erwin et al., 1998; Smith et al., 2010). Moreover, the micro- and macro-cerebrovascular alterations due to metabolic changes might also affect the integrity of the neural circuits involved in sensory gating. The principal objective of this study was thus to investigate the relationship between sensory gating deficit and metabolic syndrome in patients with schizophrenia after adjusting for key confounding factors. We hypothesized that patients with metabolic syndrome exhibit a higher rate of sensory gating deficit compared to patients without metabolic syndrome. We therefore analyzed the association between cognitive impairments and sensory gating deficit in the context of metabolic syndrome.

## 2. Methods

### 2.1. Study participants

The study evaluated all prospective patients attending daytime hospital hours in our university and psychiatric hospital over a period of 6 months from June 2012 to December 2012. The inclusion criteria were:

- Age 18–65 years old,
- Having a diagnosis of schizophrenia according to the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV-TR) criteria (American Psychiatric Association, 2000),
- Stable antipsychotic dosage for a minimum of 3 months,
- Having French as one's native language.

The exclusion criteria were:

- Having a diagnosis other than schizophrenia on Axis I of the DSM-IV, in particular concomitant drug abuse or dependence (except tobacco),
- Major non-psychiatric disease,
- Mental retardation.

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