



Testing a decades' old assumption: Are individuals with lower sensory gating indeed more easily distracted?



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ABSTRACT

The sensory gating deficits in schizophrenia have been theorized to associate with increased distractibility. We explore the potential associations between sensory and sensorimotor gating and subjective and objective indices of distraction in healthy subjects. Forty healthy males were assessed with the P50 suppression and pre-pulse inhibition of the startle reflex (PPI) paradigms. Additionally, a neurocognitive test battery was administered in a cross-over design: with/without auditory distraction. Significant effects of distraction were found in response inhibition, and verbal working memory and attention. Parameters from the PPI and P50 suppression paradigms were significantly associated with the distractor effects on strategy formation, cognitive inhibition and flexibility, visual short-term memory, and the level of subjective distraction. Subjectively reported distraction was significantly associated with verbal working memory and attention as well as executive and supervisory processes. Sensory and sensorimotor gating efficiency do not reflect the effect of distraction across executive and attention functions i.e. we did not observe a generalized distractor effect. Gating only related to the effect of distraction on strategy formation, cognitive inhibition and flexibility, as well as visual short term memory. Future studies should investigate if gating deficits affect the distractibility of the same specific cognitive functions in patients with schizophrenia.

1. Introduction

Schizophrenia is a debilitating mental disorder associated with impairments in a broad range of cognitive domains including e.g. memory (Aleman et al., 1999; Grayson et al., 2014), executive functions (Joyce et al., 2005), attention (Melcher et al., 2014; van Os and Kapur, 2009), as well as impairments in preattentive information processing (McGhie and Chapman, 1961; Venables, 1964). It has been hypothesized that a patient's reduced ability to filter out irrelevant environmental stimuli results in too many impressions reaching the brain at the same time, hereby "flooding" his or her mind (Venables, 1964). According to this hypothesis, information flooding causes increased subjective distractibility and impaired concentration of patients with schizophrenia (McGhie and Chapman, 1961). In non-clinical populations, cognitive impairments caused by environmental noise sources have been assessed using neuropsychological methods. In this context, noise induced stress has been defined as an inability of an individual to ignore, block out, or

otherwise cope with an unwanted sound or do so at a cost (Belojevic et al., 2003). A review of 31 studies in healthy populations concluded that noise stress produced negative effects on attention, working memory, inhibition of pre-potent response, and episodic memory (Wright et al., 2014).

Two psychophysiological paradigms are believed to measure the ability to filter out irrelevant information (also called "gating"): sensory gating is measured with a P50 suppression paradigm, while a pre-pulse inhibition of the startle reflex (PPI) paradigm is a measure of sensorimotor gating. Both paradigms measure the inhibition of a response to a specific stimulus as a result of a preceding stimulus. Adler et al. (1982) were the first to observe reduced P50 suppression in patients with schizophrenia and this finding has since been replicated by many others (Bramon et al., 2004; Croft et al., 2001; Oranje et al., 2013). Reduced PPI in patients with schizophrenia was first shown by Braff et al. (1978) and was later consistently confirmed (Hammer et al., 2011; Karper et al., 1996; Parwani et al., 2000). This has led to the commonly

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accepted hypothesis that reduced gating is related to the perceptual disturbances, distractibility, and positive symptoms that are usually observed in patients with schizophrenia. Although this has been the general belief for decades, to our knowledge there is only sparse and conflicting literature exploring whether reduced gating is indeed associated with increased distractibility. Jin et al. (1998) found that schizophrenia patients with high self-report of perceptual anomalies did not differ from healthy controls in P50 ratios, whereas significantly higher P50 ratios (i.e. less gating) were observed in the patients who reported less perceptual abnormalities. This study has been criticized (Light and Braff, 2000) because patients with schizophrenia may have poor insight in their disease (Linden and Godemann, 2007; Michalakeas et al., 1994). In support of the hypothesis, one study observed that patients with schizophrenia who report a high level of perceptual and cognitive disturbances also have poor P50 suppression (Croft et al., 2001). Other studies have found significant associations between the severity of impairments of attention and sensorimotor gating (Erwin et al., 1998; Karper et al., 1996). Smucny et al. (2013) examined the association between P50 suppression and auditory attention with and without distraction in patients with schizophrenia and healthy controls. They used “real-life” auditory noise intermittently during the attention task. Only the patients showed an increase in reaction time when performing the task with distraction as compared to the condition without distraction. This increase in reaction time was significantly correlated with the P50 ratio.

Patients with schizophrenia and low P50 suppression score significantly higher on perceptual modulation, over-inclusion, distractibility, and fatigue and stress, as assessed with the Sensory Gating Inventory (SGI) (Hetrick et al., 2012) compared to both patients with high P50 suppression and healthy controls (Micoulaud-Franchi et al., 2014).

The effect of noise on attention and executive functions in healthy subjects, seems to depend on the complexity of the tasks (Wright et al., 2014). It has long been recognized in noise research that individual differences in reactions to noise may have contributed to inconsistent results (Belojevic et al., 2003; Wright et al., 2014). We use the term distractor as equivalent to noise in this study.

We hypothesized that auditory distraction would differentially impair aspects of attention and executive functions in healthy subjects in line with the observed differential effects on specific episodic memory functions (Boman et al., 2005; Hygge et al., 2003). We therefore used subjective reports after each test rather than a more generalized measure of subjective distractibility. Our main question was: do healthy males with lower sensory- or sensorimotor gating show higher distractibility, either as indicated by their subjective reports or as indicated by reduction in performance on some attention and executive function tests during distraction? Due to our hypothesis several neurocognitive functions and gating measures were assessed in an exploratory manner.

1.1. Aims of the study

The aim of the current study was to examine potential associations between gating (P50 suppression and PPI) and effects of distraction on attention and executive functions in healthy subjects using objective cognitive measures and subjective reports of distractibility.

2. Methods

The study was approved by the Ethical Committee of the Capital Region of Denmark (H-3-2012-079).

2.1. Subjects

Forty healthy male subjects with a mean age of 23.6 (3.88) years ranging from 18 to 34 years were recruited through an advertisement

on the internet. The exclusion criteria were: currently smoking, subjective reports of dyslexia, color-blindness, use of any drug of abuse within the last three months, or a personal or family history (first-degree relative) of psychiatric illness. The latter was confirmed by means of a clinical interview using the Schedule of Clinical Assessment in Neuropsychiatry (SCAN), version 2,1 (Wing et al., 1990). Additionally the Adult Self Report Scale (ASRS) version 1.1 (Kessler et al., 2005) was administered. Only males were chosen for the study since gender has been shown to influence gating (Hetrick et al., 1996) and results on gender effects in noise induced cognitive change appear mixed (Boman et al., 2005; Gulian and Thomas, 1986; Wright et al., 2016, 2014). Only non-smoking subjects were included since nicotine has been shown to affect sensory and sensorimotor gating in schizophrenia patients and in healthy and smoking subjects (Adler et al., 1993; Kumari et al., 1996).

2.2. Experimental design

Each subject participated in two test sessions separated by at least 4 weeks (range: 30–37 days). Before the first assessment the above mentioned screening interviews were administered; if the participant fulfilled the inclusion criteria and none of the exclusion criteria, he was asked to sign the informed consent. The two test days started with the participants donating a urine sample for toxicology screening of cannabis, cocaine, opiates, benzodiazepines and amphetamine. Subsequently, the participants were assessed with the Copenhagen Psychophysiological Test Battery (CPTB) consisting of four paradigms: P50 suppression, PPI, Mismatch Negativity (MMN), and Selective Attention (SA) assessed in this order (Oranje et al., 2011). Given our specific research question, only P50 suppression and PPI were analyzed in the present study. The psychophysiological assessment was followed by a neurocognitive assessment. The neurocognitive test battery aimed at assessing verbal and spatial working memory as well as other executive functions and attention that previously have been found sensitive to noise stress in healthy subjects (see Wright et al., 2014 for review).

The two test days were identical, except that on one of them a radio-podcast was played as a distractor during the neurocognitive test battery. The presentation of the auditory distraction was randomized, yet balanced across participants. The subjects were instructed to focus their attention on the performance of the test and to ignore the distractor. The distractor was paused during test instructions. To minimize the acute effect of caffeine while avoiding withdrawal effects, all subjects were asked to abstain from drinking anything containing caffeine two hours before testing.

2.3. Neurocognitive assessments

The neuropsychological assessment was performed in a quiet room without external distractions. The test administrator was present at all times. Visual short-term memory was indexed by the span length derived from the Cambridge Neuropsychological Test Automated Battery (CANTAB) Spatial Span Task (SSP) (Owen et al., 1990), whereas spatial working memory and strategy formation were reflected by the total errors and the strategy score derived from the CANTAB Spatial Working Memory task (SWM) (Morris et al., 1988; Owen et al., 1990). Response inhibition was indexed by the stop signal reaction time (SSRT) derived from the CANTAB Stop Signal Task (SST) (Chamberlain et al., 2011, 2010). Sustained attention was reflected by the A' (A prime, a signal detection measure of sensitivity to the target) derived from the CANTAB Rapid Visual Information Processing task (RVP) (Coull et al., 1996; Sahakian and Coull, 1994). Verbal fluency was assessed with the category and letter fluency tasks from the Brief Assessment of Cognition in Schizophrenia (BACS) (Keefe et al., 2004) and indexed by the total number of correct words generated. Attention and auditory working memory was indexed by the number of correct answers in the Paced Auditory Serial Addition Test (PASAT) (interstimulus intervals: 2 and

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