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Early sensory processing deficits predict sensitivity to distraction in schizophrenia

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ABSTRACT

Patients with schizophrenia frequently report difficulties paying attention during important tasks, because they are distracted by noise in the environment. The neurobiological mechanism underlying this problem is, however, poorly understood. The goal of this study was to determine if early sensory processing deficits contribute to sensitivity to distracting noise in schizophrenia. To that end, we examined the effect of environmentally relevant distracting noise on performance of an attention task in 19 patients with schizophrenia and 22 age and gender-matched healthy comparison subjects. Using electroencephalography, P50 auditory gating ratios also were measured in the same subjects and were examined for their relationship to noise-induced changes in performance on the attention task. Positive symptoms also were evaluated in patients. Distracting noise caused a greater increase in reaction time in patients, relative to comparison subjects, on the attention task. Higher P50 auditory gating ratios also were observed in patients. P50 gating ratio significantly correlated with the magnitude of noise-induced increase in reaction time. Noise-induced increase in reaction time was associated with delusional thoughts in patients. P50 ratios were associated with delusional thoughts and hallucinations in patients. In conclusion, the observation of noise effects on attention in patients is consistent with subjective reports from patients. The observed relationship between noise effects on reaction time and P50 auditory gating supports the hypothesis that early inhibitory processing deficits may contribute to susceptibility to distraction in the illness.

1. Introduction

During early investigations of sensory perception in schizophrenia, McGhie and Chapman observed that patients often complained about being overwhelmed by sensory stimuli, as if they were "overflooded" with information to the point where it became impossible to focus on any specific stimulus (McGhie and Chapman, 1961). The investigators hypothesized that patients had a fundamental deficit in "the selective and inhibitory functions of attention," such that "consciousness would be flooded with an undifferentiated mass of incoming sensory data." These deficits may contribute to positive symptoms in patients, as they may "attach important meanings to insignificant events" and become sensitive to and suspicious of the environment (Weckowicz, 1958).

Distractibility in patients has since been confirmed in numerous studies that have reported increased error rates as well as increased reaction times on various tasks in the presence of irrelevant stimuli compared to controls (Grillon et al., 1990; Lawson et al., 1967; McGhie et al., 1965a,b; Payne and Caird, 1967; Steffy and Galbraith, 1975). The deficit may be especially pronounced using auditory tasks with auditory distractors (McGhie et al., 1965a; Lawson et al., 1967). Patients whose positive symptoms persist to a greater degree following treatment may be particularly susceptible to auditory distraction (Green and Walker, 1986; Walker and Harvey, 1986).

Deficits in the "inhibitory functions of attention" may arise due to several factors, including pathology of prefrontal-cortical processes involved in the voluntary control of attention (so called "top-down" effects) as well as disruptions in early sensory processes (i.e. "bottom-up" effects). Although the vast majority of research on the neurobiology of schizophrenia has focused on dysfunction in cognitive, "top-down" areas (such as the prefrontal cortex), a growing body of literature suggests that early sensory processing might also be disrupted in the illness (Javitt, 2009). Using electroencephalography (EEG), studies have consistently reported abnormalities in early (often 50 or 100 ms latency) event related potential responses (ERPs) to stimuli in patients with schizophrenia.

The P50 is an early auditory evoked response to a stimulus that exhibits reduced amplitude when a second stimulus is presented 500 ms following the first. This reduction, usually studied in the auditory domain with repeated pairs of clicks, is referred to as P50 gating and may be a mechanism for automated, early inhibitory control and filtering of responses to repetitive stimuli (Roth and Kopell, 1969), preventing organisms from being overwhelmed by redundant sensory stimulation in the environment (Croft et al., 2001). The magnitude

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of inhibition is defined as the ratio of the evoked response amplitude to the first stimulus (S1) to the evoked response amplitude of the second stimulus (S2) (i.e. S1/S1), or P50 ratio. This inhibition is often reduced or eliminated in patients with schizophrenia, demonstrating a failure in sensory gating that may be related to stimulus "overflooding" (Patterson et al., 2008). Thus, inhibitory failure of S2 suppression may be a mechanism by which patients are more distracted by irrelevant environmental stimuli.

Nonetheless, evidence that P50 gating is associated with related symptomatology (e.g. poor selective attention or perceptual abnormalities) is limited and findings are mixed. Two studies have found an association between poor sensory gating and attentional deficits (Cullum et al., 1993; Erwin et al., 1998). In contrast, another study found no association between perceptual abnormalities (assessed by interview) and P50 ratio (Jin et al., 1998). Associations between P50 ratio and working memory as well as processing speed have also been reported (Potter et al., 2006). However, to our knowledge, no study has examined the relationship between distractibility (defined here as impaired selective attention) in schizophrenia and P50 gating.

In the present study, we examined the effect of an environmentally relevant noise distraction on performance of an auditory attention task in schizophrenia patients and healthy comparison subjects. The distracting urban noise stimulus is a mixture of common sounds from the environment simulating what a person may experience in a real-life urban setting, including multiple conversations and noises recorded from a party, music, and conversations from the radio (Tregellas et al., 2009). To determine if early sensory processing contributes to the effects of distracting noise on attention, P50 auditory gating ratios were measured and examined for their relationship to noise-induced changes in performance on the attention task. We hypothesized that patients would show more pronounced performance deficits during noise, and that the magnitude of this deficit would be associated with impaired sensory gating. Additionally, given previous suggestions that distractibility may be related to positive symptoms, we hypothesize that both noise effects and P50 gating would be associated with BPRS measures of hallucinations and delusions in patients.

2. Methods

This study was approved by the Colorado Multiple Institutional Review Board. Only decisionally capable subjects with schizophrenia were eligible for study participation.

2.1. Subjects

Participants included 19 outpatients who met the DSM-IV criteria for schizophrenia (13 males, 6 females, 6 smokers, average age 47 years, standard deviation 11 years, range 20–62 years) and 22 healthy comparison subjects recruited from the local community (13 males, 9 females, no smokers, average age 42 years, standard deviation 14 years, range 22–64 years). Patients were recruited by referral from a psychiatrist involved in the study (A.O.) and by other local clinicians and mental health professionals. Groups were not significantly different with respect to gender (Mann–Whitney $U = 190$, $df = 39$, $p = 0.54$) or age ($t = 1.28$, $df = 39$, $p = 0.21$). Exclusion criteria included a current diagnosis of substance abuse, neurological disorders, or head trauma. BPRS (24-item) scores were determined by a clinician (A.O.); all patients were stable and were not being hospitalized at the time of scoring. Scores were unavailable for two patients. One patient was being treated with conventional antipsychotics, two patients with a combination of conventional and atypical antipsychotics, and the remaining patients with atypical antipsychotics. Healthy comparison subjects were excluded for Axis I disorders including schizophrenia, bipolar disorder, depression, anxiety, and lifetime substance dependence as well as a first-degree family history of psychosis. After complete description of the study to the subjects, written informed consent was obtained. Subjects were compensated for participation.

2.2. Task description

All subjects first underwent a hearing test to ensure they did not have a substantial difference (greater than 10 dB) in hearing between each ear.

Subjects performed an auditory version of the Sustained Attention to Response Task (SART) (Seli et al., 2012). For the SART, single-digit numbers were presented sequentially, and the subject was asked to respond (with a spacebar press) after each auditory stimulus (60 dB, presented in the right ear with headphones (Bose Acoustic Noise Canceling)) except for the number '3,' in which case the subject was asked to withhold from responding. The predictable nature of the stimuli minimized the requirement for stimulus-driven motor response inhibition (Dockree et al., 2004); the task also required minimal involvement of frontal executive components such as working memory or conflict monitoring (O'Grada et al., 2009). The task consisted of 126 trials (with each trial being the presentation of a single number), with a 250 ms stimulus duration and 900 ms intertrial interval. Subjects were asked to respond as quickly and accurately as possible to help induce attentiveness.

Blocks of distracting urban noise stimuli (80 dB, presented in the left ear, 10 s duration) were pseudo-randomly dispersed over half of the trials.

2.3. Auditory stimuli

For the auditory SART, synthetic audio recordings for the numbers 1–9 were downloaded from www.modeltalker.com. Number stimuli were adjusted to have the same onset with Adobe Audition.

For task-overlaid noise distraction, urban noise stimuli were mixed as described previously (Tregellas et al., 2009). Briefly, clips included segments from two talk radio shows, two classical musical pieces, sounds from a neighborhood block party, which included multiple background conversations and sounds from children playing, traffic sounds, a refrigerator motor cycling on and off, and frequent knocking sounds from glasses being set on countertops. Volumes of all of these elements were mixed so that no one element was readily identifiable. The subjective experience of the sound mixture was that of standing in a busy crowd of people, in which multiple conversations were occurring, with a low level of indistinguishable background music and other sounds.

2.4. Behavioral data analysis

Performance measures for the task were 1) %errors of commission, or the frequency of a spacebar press during presentation of the number '3' when no responses were required, 2) %errors of omission, or the frequency of the absence of a spacebar press during any number except for '3,' when responses were required, and 3) reaction time. The effect of noise on each measure was calculated by subtracting the mean value for each subject during noise from the mean value in silence. The primary measure of interest was reaction time, as previous studies have demonstrated greater effects of distracting noise on reaction time in patients compared to controls (Payne and Caird, 1967; Grillon et al., 1990).

No significant associations between age, gender, or smoking status were observed on any measures of interest; thus, results were not adjusted for these factors.

The dependent measures (percent errors of commission, percent errors of omission, and reaction time) were each entered into a 2×2 repeated measures ANOVA with distraction condition (noise or silence) as a within-subjects factor and diagnosis (patient or control) as a