Available online at www.sciencedirect.com
ScienceDirect
Schizophrenia Research 93 (2007) 288–295
SCHIZOPHRENIA RESEARCH
www.elsevier.com/locate/schres

Deficient attentional modulation of startle eyeblink is associated with symptom severity in the schizophrenia spectrum ☆

Erin A. Hazlett [a,*], Michelle J. Romero [a], M. Mehmet Haznedar [a], Antonia S. New [a,b], Kim E. Goldstein [a], Randall E. Newmark [a], Larry J. Siever [a,b], Monte S. Buchsbaum [a]

[a] *Department of Psychiatry, Mount Sinai School of Medicine, New York, NY, United States*
[b] *Department of Psychiatry, Bronx Veterans Affairs Medical Center, the Bronx, NY, United States*

Received 1 December 2006; received in revised form 2 March 2007; accepted 7 March 2007
Available online 2 May 2007

Abstract

Patients with schizophrenia-spectrum disorders show deficient prepulse inhibition (PPI) of the startle eyeblink reflex which is thought to reflect an early stage of information processing called automatic sensorimotor gating. They also exhibit deficient *attentional* modulation of PPI and prepulse facilitation (PPF) of startle which is thought to reflect deficient early and later controlled attentional processing. This is the first study to assess *attentional* modulation of PPI and PPF in a 3-group schizophrenia-spectrum sample of age- and sex-matched *unmedicated* schizotypal personality disorder (SPD) and schizophrenia patients, and healthy controls. Participants performed a tone-length judgment task involving attended, ignored, and novel tone prepulses while the acoustic startle eyeblink reflex was measured. Healthy controls showed greater PPI and PPF during the attended prepulses compared with the ignored prepulses. In contrast, both the SPD and schizophrenia patient groups failed to show this pattern, indicating deficient early and later controlled attentional processing. These findings suggest abnormal attentional modulation of PPI and PPF may be a trait-like feature found in patients with schizophrenia-spectrum disorders. Among the schizophrenia-spectrum sample, more deficient PPI during the attended prepulses was associated with greater symptom severity as measured by the total 18-item Brief Psychiatric Rating Scale score.

Keywords: Schizophrenia; Schizotypal personality disorder; Startle; Attention; Prepulse inhibition; Prepulse facilitation

1. Introduction

Startle eyeblink modification (SEM) is a useful psychophysiological tool for studying information processing by examining how the amplitude of an eyeblink resulting from a loud noise burst is modified by a preceding, non-startling stimulus (called a prepulse). When a prepulse precedes the startle pulse by a short (<500 ms) interval (known as the lead interval), the startle eyeblink amplitude is inhibited, a phenomenon known as prepulse inhibition (PPI). In contrast, when the lead interval is longer (>1000 ms), startle eyeblink amplitude is facilitated, particularly when the prepulse and startle stimulus are in the same sensory modality, a phenomenon known as prepulse facilitation (PPF). Although PPI is thought to be automatic, several studies have shown that

☆ This research was supported in part by an Independent Investigator Award to the first author from the National Alliance for Research on Schizophrenia and Depression.

* Corresponding author. Department of Psychiatry, Box 1505, Mount Sinai School of Medicine, One Gustave L. Levy Place, New York, NY 10029, United States. Tel.: +1 212 241 2779; fax: +1 212 423 0819.
E-mail address: erin.hazlett@mssm.edu (E.A. Hazlett).

0920-9964/$ - see front matter © 2007 Elsevier B.V. All rights reserved.
doi:10.1016/j.schres.2007.03.012

by directing attention toward the prepulse, PPI and PPF are enhanced (Dawson et al., 1993; Filion et al., 1993; Hawk et al., 2002; Hazlett et al., 1998, 2003; Schell et al., 2000). Thus, in an active-attention SEM paradigm PPI and PPF are thought to index early and later controlled attentional processing, respectively.

Investigators have used SEM to examine information processing deficits in schizophrenia for many years (Braff et al., 1978; Braff and Geyer, 1990; Cadenhead et al., 1997; Dawson et al., 1993; Hazlett et al., 1998). More recently, PPI has been used as a vulnerability marker or endophenotype in schizotypal personality disorder (SPD) because it provides an important way of assessing phenotypic traits that may not be evident clinically (Cadenhead et al., 2000, 2002). Similar to schizophrenia (Dawson et al., 1993, 2000; Hazlett et al., 1998), individuals with SPD (Hazlett et al., 2003) and psychosis-proneness (Schell et al., 1995) exhibit deficiencies in both early and late controlled attentional modulation of SEM. These studies suggest that deficits in the attentional modulation of SEM may be the same in SPD and schizophrenia, yet different from normal—a discrete variable or trait-linked vulnerability to disorders in the schizophrenia spectrum. Alternatively, SEM deficits may show a spectrum pattern—a continuous variable with SPD patients similar to schizophrenia but not so severe. The landmark Danish adoption studies of Kety et al. (1971) explored schizotypal characteristics in the biological relatives of schizophrenia probands and ultimately led to the concept of a "schizophrenia spectrum." Patients with SPD share with schizophrenia patients their persistent asociality and cognitive impairment, albeit to a milder degree, which presumably emerge from common spectrum-related risk factors that are both genetic and environmental (Siever et al., 2002; Siever and Davis, 2004). Yet, SPD patients also have factors which protect against the severe cognitive/social deficits and frank psychosis of chronic schizophrenia.

In medicated schizophrenia patients, greater PPI impairment during the attended prepulse has been associated with heightened positive symptoms related to thought disturbance (Dawson et al., 2000). This is consistent with the idea that individuals with better PPI during the attended prepulses are better able to focus on salient stimuli. Dawson et al. suggest that individuals less able to protect information processing when it is most needed show the greatest tendencies toward disconnected speech and delusional thought. In contrast, studies using a passive-attention paradigm do not detect symptom correlates of PPI in patients (Swerdlow et al., 2006). As noted by Swerdlow et al, this problem is likely due to "ceiling-level" symptoms and "floor-level" functioning in patients which results in restricted range.

The aim of the present study was to examine PPI and PPF during an active-attention paradigm in unmedicated patients with diagnoses in the schizophrenia spectrum and age- and sex-matched healthy controls. To our knowledge, this is the first report directly comparing attentional modulation of PPI and PPF in age- and sex-matched schizophrenia and SPD patients. We hypothesized that compared with healthy controls, (1) schizophrenia patients would show deficient early and late attentional modulation of SEM, (2) SPD patients would show abnormalities in SEM that would be similar but less marked than those observed in schizophrenia, and (3) deficient attentional modulation of PPI in the schizophrenia-spectrum would be associated with greater positive symptom severity.

2. Method

2.1. Participants

We report data from a total of 12 schizophrenia patients (5 never medicated, 7 previously medicated but off for minimum of two weeks; 9 M, 3 F, mean age = 37.3 ± 15.9), 15 SPD patients (12 never medicated, 3 received psychotropic medication in lifetime but not during the past year, 11 M, 4 F, mean age = 40.5 ± 8.5), and 14 healthy controls (9 M, 5 F, mean age = 35.0 ± 11.7). The groups did not significantly differ in age or sex distribution. Data from an additional 6 participants (2 controls, 1 SPD and 3 schizophrenia patients) were discarded due to technical problems with their SEM data (e.g., failure to blink, equipment malfunction).

The SPD patients met DSM-III-R and DSM-IV diagnostic criteria on the basis of interviews from the Schedule for Schizophrenia and Affective Disorders (Endicott and Spitzer, 1978) and the Structured Interview for DSM-III-R Personality Disorders (Pfohl et al., 1989). The schizophrenia patients met DSM-IV criteria for schizophrenia based on the Comprehensive Assessment of Symptoms and History (Andreasen et al., 1992). The healthy volunteers received the same interview as the SPD patients and those with an Axis I or II psychiatric illness in themselves or an Axis I diagnosis in a first-degree relative were excluded. To assess clinical symptoms, the Brief Psychiatric Rating Scale (Overall and Gorham, 1962) was given to all patients. Schizophrenia patients had significantly higher 18-item BPRS scores (mean = 49.7 ± 18.1, range = 30–59) compared with the SPD patients (mean = 27.3 ± 5.8, range = 19–39; $t(25) = 4.54$, $p = 0.0001$).