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The association between psychosis proneness and sensory gating in cocaine-dependent patients and healthy controls

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ABSTRACT

This was a naturalistic study of 23 abstinent cocaine-dependent patients and 38 controls who were studied using a paired-stimulus paradigm to elicit three mid-latency auditory evoked responses (MLAERs), namely, the P50, N100, and P200. Sensory gating was defined as the ratio of the S2 amplitude to the S1 amplitude. Psychosis-proneness was assessed using four Chapman psychosis proneness scales measuring perceptual aberration, magical ideation, social anhedonia, and physical anhedonia. Omnibus correlations based upon the entire sample revealed significant and differential relationships between the MLAER components and psychosis-proneness. Social Anhedonia scale scores accounted for the largest proportion of variance in the P50 gating ratio, while Perceptual Aberration scores accounted for the largest proportion of variance in P200 gating. Psychosis proneness and sensory gating appear to be associated. In particular, poorer P50 gating is related to higher scores on the Social Anhedonia scale in healthy controls and across mixed samples of cocainede-pendent patients and controls. These findings hold significance for the further understanding of the relationship between deficient sensory gating ability and the propensity to developing psychotic symptoms in a vulnerable population like cocaine-dependent individuals.

1. Introduction

Sensory gating, the ability of the central nervous system to inhibit or attenuate incoming redundant stimuli, is proposed to be a major mechanism for the protection of the subject's internal environment as well as their higher cortical centers from being flooded with irrelevant information (Venables, 1964). One of the most commonly studied measures of sensory gating is the attenuation of the amplitude of the P50 with stimulus repetition. The P50 is an early positive component of the mid-latency auditory evoked responses (MLAERs) occurring between 45 and 90 ms post-stimulus onset. While the P50 component of the MLAERS reflects the preattentive stage of information processing, early and later attentive phases of information processing are reflected by the N100 and P200 components, respectively. A growing literature reveals that the well-documented P50 sensory gating deficit of schizophrenia patients extents to these later phases of information processing (Smith et al., 2010; Turetsky et al., 2009). Schizophrenia patients display significantly decreased N100 gating (Boutros et al., 1999, 2009, 2004b; Clementz and Blumenfeld, 2001; Clementz et al., 2003) and P200 gating (Boutros et al., 2009, 2004b) relative to healthy controls. Although relatively little is known regarding the clinical correlates of the sensory gating deficits in schizophrenia-spectrum patients, one hypothesis is that the sensory gating deficits may be related to psychosis-proneness. Schizotypal personality disordered patients display similar P40 deficits as schizophrenia patients (Cadenhead et al., 2000; Croft et al., 2001).

1.1. Sensory gating in non-clinical populations

To date, a number of studies have examined the relationship between schizotypy and sensory gating in nonclinical populations. However, the methodological shortcomings of much of this work limit the conclusions that can be drawn. Using a convenience sample of volunteers at a medical school, Croft et al. (2001) observed that participants with higher schizotypal characteristics namely, perceptual experiences and magical ideation, exhibited poorer P50 suppression. When smoking status was assessed, Croft et al. (2001) found a difference in patterns of associations between lighter and heavier smokers, whereby lighter smokers showed a positive association between positive schizotypy and poor P50 suppression. One criticism of both of these studies, however, is that schizotypy was assessed using the Personality Syndrome Questionnaire (Gruzelier et al., 1995),

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a questionnaire for which there are no published psychometric data available (Evans et al., 2007). In contrast to the Croft et al. (2001, 2001) findings, Wang et al. (2004) observed that negative schizotypy (i.e., the "withdrawn" dimension as measured by the Raine (1991) Schizotypal Personality Questionnaire) was associated with poor P50 suppression. The smoking status of the nonclinical volunteers in the Wang et al. (2004) study was not provided. Furthermore, in the Wang et al. (2004) study, the investigators used a shorter (e.g., 250 ms) than the usual 500 ms interstimulus interval; it is unclear whether this may have affected the findings. A later study conducted by Wan et al. (2008) also used Raine's Schizotypal Personality Questionnaire to assess schizotypy, and improved upon prior studies by allowing a comparison of smokers vs. nonsmokers in both high and low schizotypal groups. Unfortunately, the investigators failed to exclude participants on the basis of their family history, so that both the high and low schizotypal groups included participants who had first degree relatives with schizophrenia. This presented a major confound, given that P50 nonsuppression is also observed among first degree relatives of schizophrenia patients (Siegel et al., 1984; Waldo et al., 1988), rendering it difficult to interpret the study findings. It should also be noted that all of the aforementioned studies had rather modest sample sizes of generally young adults. Evans et al. (2007) assessed the relationship between schizotypy, P50 and N100 suppression in a relatively large sample of healthy non-smoking undergraduates. Using the Oxford-Liverpool Inventory of Feelings and Experiences (O-LIFE; (Mason et al., 1995)), a psychometrically sound multidimensional measure of schizotypy, the investigators found a significant negative relationship between P50 suppression and cognitive disorganization. Their analyses did not reveal any significant relationships between N100 suppression and schizotypy. Overall, in healthy nonclinical populations, there appears to be a relationship between reduced P50 suppression and psychometric indicators of schizotypy, though the precise nature of the relationship is far from clear. The converging evidence suggests that reduced P50 suppression is related to schizotypy, broadly defined.

1.2. Cocaine-induced psychosis

Cocaine-induced psychosis is rare compared to the frequency of cannabis- and amphetamine-induced psychoses (Thirthalli and Benegal, 2006). Schuckit (2006) reported that although stimulant-induced psychoses typically clear within 30 days of abstinence from the psychoactive substance, some psychotic symptoms may persist beyond 4–6 weeks of abstinence in up to 15% of patients with stimulant-induced psychoses. Currently, it is unclear whether the persisting symptoms in this subgroup of patients reflect a precipitation of longer-term psychosis in predisposed individuals. Alternatively, the heavy use of stimulants might cause neurochemical changes associated with long-term psychotic disorders in individuals even if they were no predisposed to psychosis (Philgren and Boutros, 2007). Prior work indicates that cocaine-dependent patients display abnormal P50 suppression relative to healthy controls (Boutros et al., 2000; Fein et al., 1996). Additionally, preliminary work from our lab (Boutros et al., 2002) suggests that in cocaine-dependent individuals, none of whom had first-degree relatives with psychotic disorders, deficient P50 sensory gating may be associated with psychosis-proneness.

Psychosis proneness is a hypothesized construct indicating elevated risk for any form of psychosis. Theoretically, individuals with elevated psychosis-proneness may later manifest a number of psychotic disorders, including schizophrenia, schizoaffective disorder, bipolar disorder, delusional disorder, and drug-induced psychoses. Psychosis proneness has been extensively studied using psychometric indicators of risk such as scales developed by Loren and Jean Chapman. Longitudinal investigation reveals that the Perceptual Aberration Scale (Chapman et al., 1994) identifies a subgroup of psychosis-prone individuals, some of whom eventually manifest a psychotic disorder. These individuals had a heterogeneous outcome, with a heightened prevalence of psychotic disorders including, but not limited to schizophrenia (i.e., some individuals developed nonschizophrenia-related psychotic disorders such as delusional disorders and psychotic mood disorders). Analysis of the Chapmans' longitudinal study of psychosis-prone individuals (Kwapil, 1998) as well as a more recent longitudinal study utilizing an independent sample (Gooding et al., 2005) indicates that individuals with aberrantly high scores on the revised Social Anhedonia Scale are at heightened risk for the later development of schizophrenia-spectrum disorders. Thus, the Social Anhedonia Scale, unlike the Perceptual Aberration Scale, may identify individuals at specific risk for the development of schizophrenia-spectrum disorders. To date, the psychosis-proneness scales developed by Chapman and their associates remain the sole psychosis-proneness scales to be longitudinally validated to predict the later development of schizophrenia (Chapman et al., 1994; Kwapil, 1998) and/or schizophrenia-spectrum disorders (Gooding et al., 2005, 2007; Kwapil, 1998).

1.3. The present study

The goal of the present investigation were twofold: first, to investigate the clinical correlates of sensory gating indices derived from an early mid-latency auditory evoked potential believed to reflect pre-attentive processes (the P50) and the N100/P200 MLAER components believed to be more under the influence of attentive processes, in healthy controls and in abstinent cocaine-dependent patients. By investigating P50, N100, and P200 in healthy controls, we intended to examine factors related to the clinical correlates of sensory gating in general. Through our study of P50, N100, and P200 in abstinent cocaine-dependent patients using longitudinally validated measures of psychosis-proneness, we sought to examine possible underlying factors relating to the development of psychosis in the context of cocaine use. It is not currently known whether cocaine-dependence exposes an underlying psychosis diathesis, or whether psychotic symptoms are induced by stimulant use. At least one aspect of psychosis-proneness, namely, schizotypy, is thought to be trait-based (see, e.g., (Meehl, 1962, 1989)). If cocaine-dependence exposes an underlying psychosis diathesis, one might expect associations between psychosis-proneness and sensory gating, similar to the relationships observed among individuals with schizophrenia-related psychoses, all of whom possess schizotypy. Alternatively, if the psychotic symptoms are induced by stimulant use, we would not expect a relationship between measures of psychosis-proneness and sensory gating, but rather we would expect higher endorsements of psychotic-like experiences namely, perceptual aberrations and magical ideations, in patients with longer duration and/or greater severity of stimulant use. As such, given the goal to explore the relationship between psychometric indicators of schizotypy and electrophysiological markers of brain functioning in individuals with and without cocaine-induced psychosis, it was advantageous to use measures with documented predictive validity. We had two a priori hypotheses, namely, that deficient sensory gating in cocaine-dependent subjects would extend beyond the P50 stage of information processing, and secondly, that across both groups, P50 sensory gating deficits would be associated with psychometric indicators of schizotypy, namely, social anhedonia.

2. Methods

2.1. Participants

2.1.1. Patients

The sample consisted of 61 participants (23 patients and 38 healthy controls). The patients (10 males and 13 females; a mean age of 36.52 years) met DSM-IV (APA, 1994) criteria for cocaine dependence during the past year and had been free