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Event-related potentials demonstrate deficits in acoustic segmentation in schizophrenia

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ABSTRACT

Segmentation of the acoustic environment into discrete percepts is an important facet of auditory scene analysis (ASA). Segmentation of auditory stimuli into perceptually meaningful and localizable groups is central to ASA in everyday situations; for example, separation of discrete words from continuous sentences when processing language. This is particularly relevant to schizophrenia, where deficits in perceptual organization have been linked to symptoms and cognitive dysfunction. Here we examined event-related potentials in response to grouped tones to elucidate schizophrenia-related differences in acoustic segmentation. We report for the first time in healthy subjects a sustained potential that begins with group initiation and ends with the last tone of the group. These potentials were reduced in schizophrenia, with the greatest differences in responses to first and final tones. Importantly, reductions in sustained potentials in schizophrenia patients were associated with greater negative symptoms and deficits in IQ, working memory, learning, and social cognition. These results suggest deficits in auditory pattern segmentation in schizophrenia may compound deficits in many higher-order facets of the disorder.

1. Introduction

Separation of acoustic events into discrete percepts, or auditory scene analysis (ASA), is accomplished through segregation of multiple sources/streams, integration of concomitant acoustic elements, and segmentation of stimuli within a stream into auditory objects (Bregman, 1990). Segmentation of stimuli into perceptually meaningful objects is crucial in everyday situations; for example, the separation of discrete words from continuous language. Neurophysiological studies using event-related potentials (ERPs) suggest acoustic segmentation in auditory cortex is not dependent upon attention (Näätänen et al., 2001). Atienza et al. (2003) demonstrated that the mismatch negativity (MMN) ERP can be reduced or eliminated by changing temporal relationships between tone sets, thereby eliminating the perception of discrete auditory objects. Sussman and Gumenyuk (2005) also showed that temporal relationships within tone sets can affect whether tones are grouped as objects. Further, MMN is also elicited when established patterns are violated in auditory groups, such as changes in the number of tones (Salisbury, 2012; Van Zuijen et al., 2004; Rudolph et al., 2015), or pitch relationships between tones (Saarinen et al., 1992). Although these studies clearly demonstrate effects of acoustic segmentation, a more direct measure is needed which does not rely on pattern deviation.

Segmentation is relevant to schizophrenia, where deficits in perceptual organization are related to poor functional outcome (Uhlhaas and Silverstein, 2005). Schizophrenia patients have pronounced deficits in working memory and attention (Silver et al., 2003; Nuechterlein et al., 2004), which are central to ASA (Scott, 2005). Also, schizophrenia patients are slower to learn visual sequences in a serial reaction time task (Adini et al., 2015). Behavioral and electrophysiological evidence suggests impairment in the ability to perceptually segregate auditory streams in schizophrenia (Weintraub et al., 2012; Ramage et al., 2012); however, effects of schizophrenia on electrophysiological indices of segmentation of acoustic patterns into auditory objects has not been studied. In this paper, we identify the electrophysiological correlates of acoustic segmentation in healthy subjects and identify deficits in these measures in schizophrenia.

In behavioral studies of auditory pattern recognition, tones presented in first and last positions in a pattern are more easily recognized than intermediate tones (Macken et al., 2003; Mondor and Morin, 2004). Additionally, single-neuron recordings from primary and secondary auditory cortex in the cat have identified neurons that preferentially respond to tones in first and last positions (McKenna et al., 1989). We hypothesized that ERP amplitudes to first and last tones in a group would differ from responses to intermediate tones, and that ERP indices of segmentation would be reduced in schizophrenia. Deficits in visual perceptual organization exist in schizophrenia (Uhlhaas and Silverstein, 2005), but little is known about the perception of auditory

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Table 1
Participant characteristics. Mean values are reported with standard deviations in parentheses. Asterisks represent significant differences between groups (*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$). All other differences are non-significant with $p > 0.1$.

	Patients	Controls
Socio-demographic data		
N	24	22
Age (years)	35.5 (8.7)	32.4 (10.8)
Sex (M/F)	17/7	13/9
Education (years)***	13.1 (2.4)	15.8 (2.7)
Participant SES***	29.9 (14.0)	45.2 (10.7)
Parental SES	34.9 (15.3)	41.7 (9.5)
WASI IQ	101.6 (13.3)	107.6 (11.2)
Age at onset (years)	21.4 (7.8)	
Duration of illness (years)	14.0 (6.9)	
Clinical data (T-scores)		
PANSS — positive symptoms	42.2 (8.4)	
PANSS — negative symptoms	47.9 (10.2)	
PANSS — total	44.3 (7.6)	
BACS***	35.6 (12.6)	52.3 (11.7)
MCCB — processing speed***	34.1 (12.1)	54.5 (10.3)
MCCB — attention**	37.4 (12.7)	49.2 (7.8)
MCCB — working memory*	37.3 (11.7)	45.0 (6.9)
MCCB — verbal learning***	35.9 (8.5)	53.4 (9.2)
MCCB — visual learning*	37.7 (11.6)	45.0 (8.9)
MCCB — reasoning/problem solving*	45.3 (10.9)	51.8 (7.1)
MCCB — social cognition***	35.3 (13.8)	53.4 (7.7)
MCCB — total***	30.7 (13.3)	50.4 (7.2)
Medication data		
Chlorpromazine equivalent dose (mg)	529 (292)	
Medicated/unmedicated	23/1	

groups. As deficits in other electrophysiological signs of auditory perceptual processes are prominent in schizophrenia (Salisbury et al., 2010; Javitt, 2009a; Foxe et al., 2011), we expected the same for ERP indices of acoustic segmentation.

2. Materials and methods

2.1. Participants

Twenty-five individuals with schizophrenia (Sz) and 22 healthy control subjects (HC) participated in this study. One Sz participant was excluded from analysis (N = 46, see Section 2.5). Subjects were matched for age, gender, and parental social economic status (Table 1). Subjects had normal hearing as assessed by audiometry and received $50 for participation. The study was approved by the University of Pittsburgh IRB.

2.2. Procedures

EEG was recorded while participants watched a silent video. Binaural tones created with Tone Generator (NCH) were presented using Presentation (Neurobehavioral Systems) over Etymotic 3A insert earphones. In Experiment 1, six tones (75 dB, 50 ms pips, 5 ms rise/fall times, 330 ms SOA) were presented, with an initial 1.5 kHz tone, followed by 5 tones increasing in pitch in 0.5 kHz steps (final tone pitch = 4 kHz). Sets were separated by 800 ms. Deviant trials (10%)

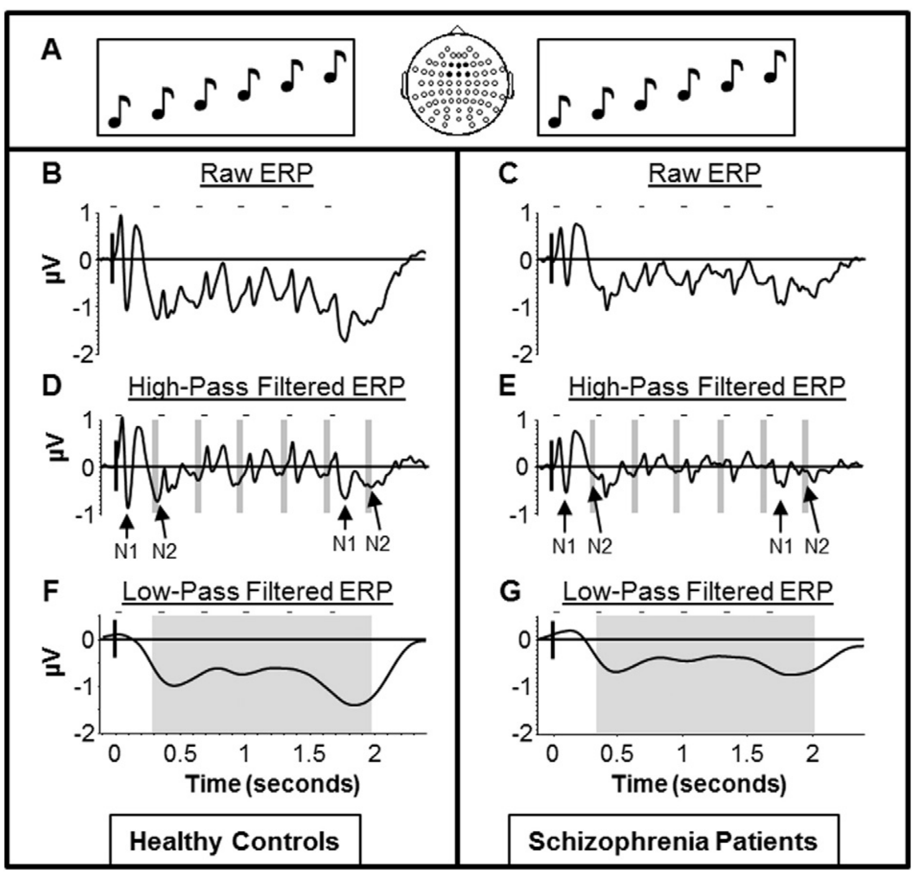

Fig. 1. Analysis of event-related potentials (ERPs) in Experiment 1. (A) A schematic depiction of an individual trial is shown in the top panels. Timing of individual tones is further represented by dashes at the top of panels B–G to orient the reader. Grand-averaged, unfiltered ERPs recorded over medial frontal electrodes are shown in (B–C), followed below by high-pass filtered (>1.5 Hz) grand-averaged ERPs (D–E), and low-pass filtered (<1.5 Hz) grand-averaged ERPs (F–G). N1 and N2 responses to the first and final tones are highlighted to orient the reader (arrows). N2 amplitudes were extracted from shaded areas in high-pass filtered ERPs (D–E). Sustained potential amplitudes were extracted from shaded areas low-pass filtered ERPs (F–G). ERPs from healthy controls are shown in left panels and ERPs from schizophrenia patients are shown in right panels. Channels from which average ERP waveforms were calculated are shown at the top right corner of the figure.