Abstract

Smell identification deficits (SIDs) are relatively specific to schizophrenia and its negative symptoms, and may have predictive value for conversion to high-risk individuals (Corcoran et al., 2009). Moreover, event-related potentials (ERPs) to odors are reduced in schizophrenia, and may be absent in prodromal patients. This study examined whether prodromal patients show SIDs and abnormal olfactory N1 and P2 potentials seen in schizophrenia. Methods: 49-channel ERPs were recorded from 21 prodromal and 20 healthy adolescents (13/13 male; age 21.4±3.5, range 13-27 years) during an odor detection task using three concentrations (strong, medium, weak) of hydrogen sulfide (H2S) or blank air presented unilaterally and analyzed with a constant-flow olfactometer (variable ISI 15-21 s). Subjects indicated odor presence via foot pedal. Neuronal generator patterns underlying olfactory ERPs were identified and measured by unrestricted VariMAX-PCA of reference-free current source densities (CSD; spherical spline interpolation). Results: Replicating previous findings (Kayser et al., 2010), CSD waveforms to H2S stimuli were characterized by an early N1 sink (345 ms, bilateral centroparietal) and a late P2 source (580 ms, mid-fronto-temparal). N1 and P2 varied monotonically with odor intensity (strong > medium > weak) and did not differ across groups. Patients and controls also showed comparable odor detection accuracy and had normal odor identification and thresholds (Sniffin’ Sticks). Conclusions: Olfactory ERPs directly reflected differences in odor intensity, but there was no evidence of impaired olfactory processing in prodromal patients. Although this contrasts with findings for schizophrenia, it remains to be seen whether olfactory measures may be helpful in predicting conversion to psychosis.

Introduction

Olfactory function deficits are common in schizophrenia (e.g., Huby et al., 2010), and may provide a marker of disease in high-risk individuals (Corcoran et al., 2009). Olfactory deficits presumably originate from brain structures also linked to cognitive and emotional disturbances in schizophrenia. Neuropsychological studies of olfactory function indicate that event-related potentials (ERPs) to odors are abnormal (i.e., N1 and P2 amplitudes) in schizophrenia (Turetsky et al., 2010). Kayser et al. (2010) and also abnormal in their unaffected first-degree relatives (Turetsky et al., 2006).

Surface Potentials (ERP)

Current Source Densities (CSD)

Current Source Densities (CSD)

Fig. 1. Mean (SEM) percentage of correctly detected applying binomial tests (blank scored as “not detected”). Whereas both healthy controls and prodromal patients showed somatosensory changes in response to olfactory stimuli, they were breathing normally. Patients and controls also showed comparable odor detection accuracy and had normal odor identification and thresholds (Sniffin’ Sticks). Conclusions: Olfactory ERPs directly reflected differences in odor intensity, but there was no evidence of impaired olfactory processing in prodromal patients. Although this contrasts with findings for schizophrenia, it remains to be seen whether olfactory measures may be helpful in predicting conversion to psychosis.

Fig. 2. Three prodromal patients who converted to psychosis revealed marked reductions in P2 amplitude (weak, medium, and strong) compared to controls (weak, medium, and strong). N1 sinks are extremely sensitive to high risk individuals (Corcoran et al., 2009). In prodromal individuals, N1 sinks were larger than in controls. In contrast, P2 sinks were smaller in patients compared to controls. This suggests that olfactory ERPs are abnormal in prodromal patients and healthy controls.

Fig. 3. Grand average CSD waveforms for weak, medium, and strong H2S stimuli in healthy controls and schizophrenia patients in a different paradigm (Kayser et al., 2010). ERP Recording and Data Analysis

- EEG data acquired at 51.2 Hz band pass (99 dB/octave), 200 samples.
- Blink reduction (continuous EEG using epoching SVD). Interpolated horizontal and vertical EOGs, horizontal eye artifacts (peaked EEG) by linear regression of horizontal EOG (Sniffin’ Sticks). Unrestricted PCA solution using olfactory CSD waveforms. The time courses of the factor loadings identified two factors corresponding to sinks and sources associated with the olfactory N1/P2 complex (i.e., peak latencies between 200-650 ms).

Fig. 4. Unrestricted PCA solution using olfactory CSD waveforms. The time courses of the factor loadings identified two factors corresponding to sinks and sources associated with the olfactory N1/P2 complex (i.e., peak latencies between 200-650 ms).

Fig. 5. Unrestricted PCA solution using olfactory CSD waveforms. The time courses of the factor loadings identified two factors corresponding to sinks and sources associated with the olfactory N1/P2 complex (i.e., peak latencies between 200-650 ms). ERP Recording and Data Analysis

- EEG data acquired at 51.2 Hz band pass (99 dB/octave), 200 samples.
- Blink reduction (continuous EEG using epoching SVD). Interpolated horizontal and vertical EOGs, horizontal eye artifacts (peaked EEG) by linear regression of horizontal EOG (Sniffin’ Sticks). Unrestricted PCA solution using olfactory CSD waveforms. The time courses of the factor loadings identified two factors corresponding to sinks and sources associated with the olfactory N1/P2 complex (i.e., peak latencies between 200-650 ms).

Fig. 6. N1 sinks factor (345 ms) topographies revealed distinct bilateral fronto-temporal sinks in healthy controls and patients which were not correlated with odor intensity and using EEG analysis (see Fig. 5).

Fig. 7. N2 sinks factor (580 ms) topographies revealed distinct bilateral fronto-temporal sinks in healthy controls and patients which were not correlated with odor intensity and using EEG analysis (see Fig. 5). ERP Recording and Data Analysis

- EEG data acquired at 51.2 Hz band pass (99 dB/octave), 200 samples.
- Blink reduction (continuous EEG using epoching SVD). Interpolated horizontal and vertical EOGs, horizontal eye artifacts (peaked EEG) by linear regression of horizontal EOG (Sniffin’ Sticks). Unrestricted PCA solution using olfactory CSD waveforms. The time courses of the factor loadings identified two factors corresponding to sinks and sources associated with the olfactory N1/P2 complex (i.e., peak latencies between 200-650 ms).

Fig. 8. Three prodromal patients who converted to psychosis revealed marked reductions in P2 amplitude (weak, medium, and strong) compared to controls (weak, medium, and strong). N1 sinks are extremely sensitive to high risk individuals (Corcoran et al., 2009). In prodromal individuals, N1 sinks were larger than in controls. In contrast, P2 sinks were smaller in patients compared to controls. This suggests that olfactory ERPs are abnormal in prodromal patients and healthy controls.

Fig. 9. Three prodromal patients who converted to psychosis revealed marked reductions in P2 amplitude (weak, medium, and strong) compared to controls (weak, medium, and strong). N1 sinks are extremely sensitive to high risk individuals (Corcoran et al., 2009). In prodromal individuals, N1 sinks were larger than in controls. In contrast, P2 sinks were smaller in patients compared to controls. This suggests that olfactory ERPs are abnormal in prodromal patients and healthy controls.

Fig. 10. Three prodromal patients who converted to psychosis revealed marked reductions in P2 amplitude (weak, medium, and strong) compared to controls (weak, medium, and strong). N1 sinks are extremely sensitive to high risk individuals (Corcoran et al., 2009). In prodromal individuals, N1 sinks were larger than in controls. In contrast, P2 sinks were smaller in patients compared to controls. This suggests that olfactory ERPs are abnormal in prodromal patients and healthy controls.

Fig. 11. Three prodromal patients who converted to psychosis revealed marked reductions in P2 amplitude (weak, medium, and strong) compared to controls (weak, medium, and strong). N1 sinks are extremely sensitive to high risk individuals (Corcoran et al., 2009). In prodromal individuals, N1 sinks were larger than in controls. In contrast, P2 sinks were smaller in patients compared to controls. This suggests that olfactory ERPs are abnormal in prodromal patients and healthy controls.

Fig. 12. Three prodromal patients who converted to psychosis revealed marked reductions in P2 amplitude (weak, medium, and strong) compared to controls (weak, medium, and strong). N1 sinks are extremely sensitive to high risk individuals (Corcoran et al., 2009). In prodromal individuals, N1 sinks were larger than in controls. In contrast, P2 sinks were smaller in patients compared to controls. This suggests that olfactory ERPs are abnormal in prodromal patients and healthy controls.

Fig. 13. Three prodromal patients who converted to psychosis revealed marked reductions in P2 amplitude (weak, medium, and strong) compared to controls (weak, medium, and strong). N1 sinks are extremely sensitive to high risk individuals (Corcoran et al., 2009). In prodromal individuals, N1 sinks were larger than in controls. In contrast, P2 sinks were smaller in patients compared to controls. This suggests that olfactory ERPs are abnormal in prodromal patients and healthy controls.

Fig. 14. Three prodromal patients who converted to psychosis revealed marked reductions in P2 amplitude (weak, medium, and strong) compared to controls (weak, medium, and strong). N1 sinks are extremely sensitive to high risk individuals (Corcoran et al., 2009). In prodromal individuals, N1 sinks were larger than in controls. In contrast, P2 sinks were smaller in patients compared to controls. This suggests that olfactory ERPs are abnormal in prodromal patients and healthy controls.

Fig. 15. Three prodromal patients who converted to psychosis revealed marked reductions in P2 amplitude (weak, medium, and strong) compared to controls (weak, medium, and strong). N1 sinks are extremely sensitive to high risk individuals (Corcoran et al., 2009). In prodromal individuals, N1 sinks were larger than in controls. In contrast, P2 sinks were smaller in patients compared to controls. This suggests that olfactory ERPs are abnormal in prodromal patients and healthy controls.

Fig. 16. Three prodromal patients who converted to psychosis revealed marked reductions in P2 amplitude (weak, medium, and strong) compared to controls (weak, medium, and strong). N1 sinks are extremely sensitive to high risk individuals (Corcoran et al., 2009). In prodromal individuals, N1 sinks were larger than in controls. In contrast, P2 sinks were smaller in patients compared to controls. This suggests that olfactory ERPs are abnormal in prodromal patients and healthy controls.

Fig. 17. Three prodromal patients who converted to psychosis revealed marked reductions in P2 amplitude (weak, medium, and strong) compared to controls (weak, medium, and strong). N1 sinks are extremely sensitive to high risk individuals (Corcoran et al., 2009). In prodromal individuals, N1 sinks were larger than in controls. In contrast, P2 sinks were smaller in patients compared to controls. This suggests that olfactory ERPs are abnormal in prodromal patients and healthy controls.

Fig. 18. Three prodromal patients who converted to psychosis revealed marked reductions in P2 amplitude (weak, medium, and strong) compared to controls (weak, medium, and strong). N1 sinks are extremely sensitive to high risk individuals (Corcoran et al., 2009). In prodromal individuals, N1 sinks were larger than in controls. In contrast, P2 sinks were smaller in patients compared to controls. This suggests that olfactory ERPs are abnormal in prodromal patients and healthy controls.