Electrophysiologic evidence for olfactory dysfunction in schizophrenia: A CSD-PCA study using hydrogen sulfide

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Abstract

Deficits in olfactory threshold sensitivity, discrimination and identification are common in schizophrenia, presumably originating from limbic brain structures (e.g., orbitofrontal cortex, amygdala, piriform cortex) that are also linked to their cognitive and emotional dysfunctions. To study the neurophysiologic processes underlying olfactory dysfunction in schizophrenia, nasoseptal 30-channel ERP waveforms were recorded from 32 schizophrenia patients and 35 healthy adults (18/18 male) during odor detection of hydrogen sulfide stimuli presented for 200 ms to the left or right nostril at concentrations of 50% or 100% by a constant-flow olfactometer (variable 15±25 s ± 5). Time of odor stimulation was not used. Patients indicated when they perceived a low or high odor intensity. Patients with schizophrenia (percentage of missed responses) was not different from healthy controls for high (25% ± 6%) vs. low (45% ± 5%) intensity stimuli. However, temporal principal components analysis (unrestricted Varimax rotation of covariance matrix) of the CSD waveforms revealed two distinct CSD factors corresponding to N1 and P2 source waves with higher intensity for both patients and controls. In agreement with findings by Turetsky et al (2003), N1 and P2 source waves were markedly reduced in patients for both odor intensities, providing electrophysiologic evidence of olfactory dysfunction in schizophrenia. The CSD-PCA methodology uniquely revealed neuronal generator patterns underlying olfactory dysfunction that are obscured by volume-conducted, reference-biased surface potentials.

Introduction

Olfactory function deficits are common in psychiatric disorders: review and methodological considerations.


DSM-IV Criteria

Schizophrenia, residual (n=1)

Schizoaffective Disorder, bipolar (n=3)

Schizoaffective Disorder, depressive (n=3)

Medication Status

Unmedicated > 14 days

Quetiapine (n=1)

Risperidone (n=7)

Perphenazine (n=2)

Behavioral Data

Mean (SEM) percentage of missed responses

Healthy Adults = 35

Schizophrenic Patients = 32


ERP Recording and Data Analysis

- ERPs recorded from 30 scalp placements using an electrode cap with a nose-reference, 250-2000 ms
- BIS-data acquired at ±3.0 for band pass (Deflective, Broad horizontal and vertical EOG, blink rejection, (Continuous EEG) using spatial SVD horizontal orientation surfaces (offset electrodes) at one pre-stimulus and 100 ms post-stimulus, eyes closed)
- ERPs re-referenced to linked mastoids (TP9/10), averages (artifact-free trials, correct responses only) low pass filtered at 10Hz (12.5 Hz for 200 ms), band pass filtered (30-450 Hz), after spatio-spatial ICA of the covariance matrix (201 variables = stimulus-locked samples 250 to 1,750 ms; 4,154 observations = 1 Hz frequency bin).

CSD-PCA Factor Loadings and Scores

CSD components revealed highly significant intensity effects across groups. Patients’ performance was not different from controls for both odor intensities. High-voltage CSD factors corresponding to N1 and P2 source waves were submitted to repeated measures ANOVA (gender, diagnosis, and gender * diagnosis, male vs. female) as between-subject factors, and CSD factors as within-subject factors. ANOVA design allowed interaction terms of lateral, hemispheric recording sites over both hemispheres at which PCA factor scores were largest and were representative of the ascended CSD component(s) (Kayser & Tenke 2003). N1 sink generator pattern appears to be unique for olfactory stimuli, whereas P2 source waveforms are highly comparable to those found in schizophrenic patients. However, both groups showed comparable intensity-related effects on both CSD components.

Surface Potentials

- Patients and controls produced highly comparable ERP/CSD waveform topographies (Fig. 2-4).
- N1 sink (305) was more clearly defined in healthy adults than in schizophrenia.
- P2 source (630) was more pronounced in schizophrenia than in healthy adults. The N1 sink generator pattern appears to be unique for olfactory stimuli, whereas P2 source waveforms are highly comparable to those found in schizophrenic patients. However, both groups showed comparable intensity-related effects on both CSD components.

Summary and Conclusions

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- N1 sink (305) was more clearly defined in healthy adults than in schizophrenia.
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- The N1 sink generator pattern appears to be unique for olfactory stimuli, whereas P2 source waveforms are highly comparable to those found in schizophrenic patients. However, both groups showed comparable intensity-related effects on both CSD components.

CSD-PCA methodology can clarify the basic component structure of olfactory ERPs.