

NEURONAL GENERATOR PATTERNS OF EVENT-RELATED POTENTIALS (ERPs) TO PLEASANT AND UNPLEASANT ODORS IN DEPRESSED AND HEALTHY ADULTS

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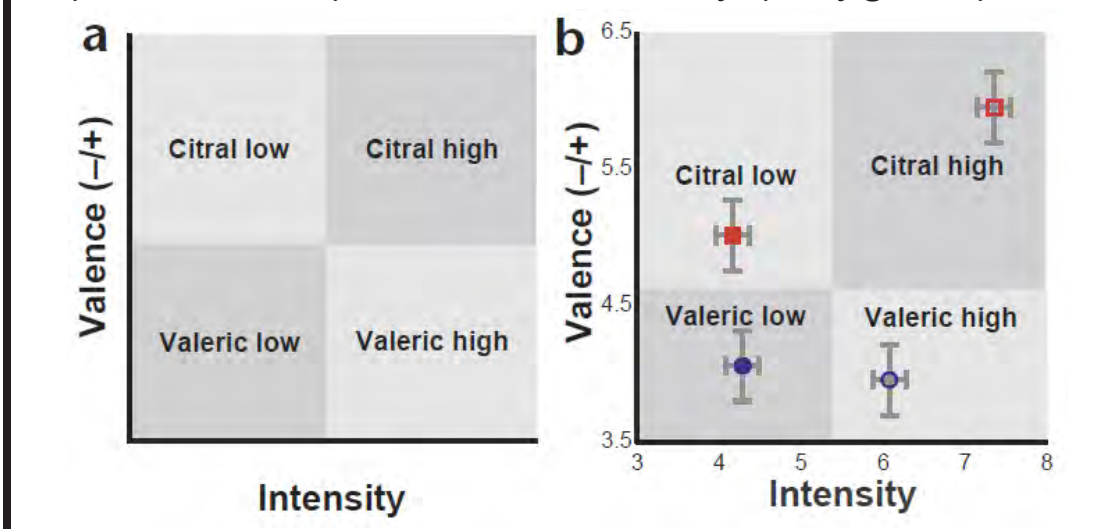
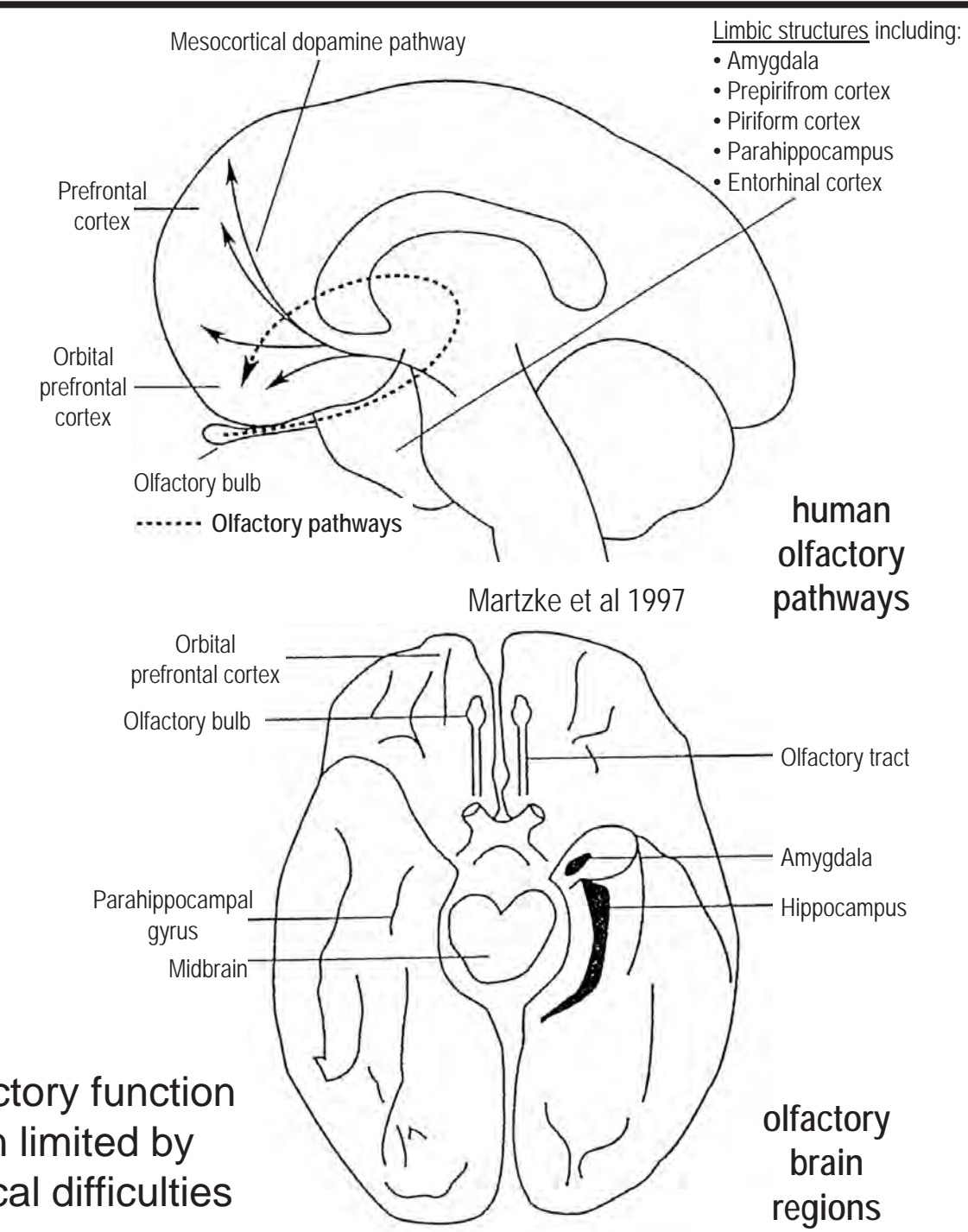
Poster available in high resolution at
<http://psychophysiology.cpmc.columbia.edu/mmmedia/spr2011/oeerpemot.pdf>

Abstract

Background: Despite the overlap of cortical and limbic structures involved in olfaction, emotion and depression, there has been little study of olfactory function in depressed patients. **Methods:** Nose-referenced 49-channel ERPs were recorded from 25 clinically-depressed and 27 healthy adults (11/11 male) during an odor detection task using pleasant (Citronalva; CIT) and unpleasant (hydrogen sulfide; H₂S) stimuli. High or low odor concentrations or blank air were presented unilaterally by a constant-flow olfactometer (variable ISI 15-21 s). Subjects indicated odor presence via foot pedal. Neuronal generator patterns underlying ERPs were identified and measured by unrestricted Varimax-PCA of reference-free current source densities (CSD). **Results:** CSD waveforms were characterized across odors by an early sink (320 ms, bilateral frontotemporal, N1) and two distinct sources (490 ms, mid-frontocentral; 735 ms, mid-centroparietal, P2). Whereas N1 sink varied with odor intensity, P2 source varied with odor quality (H₂S > CIT). CSD amplitude and topography were highly correlated with individual ratings of valence (P2) and arousal (N1). However, CSD waveforms and topographies did not differ between groups. Likewise, patients showed normal odor identification and thresholds (Sniffin' Sticks), and did not differ from controls in behavioral performance for all conditions (76-90% vs. 74-91% correct). **Conclusions:** Although CSD measures directly reflected valence and arousal properties of pleasant and unpleasant odors, there was no evidence of impaired olfactory/emotional processing in depression.

Introduction

Given the overlap of cortical and limbic structures involved in olfaction, emotion and depression, the study of olfaction may hold particular promise for elucidating neurophysiologic dysfunctions associated with abnormalities of emotional reactivity in depression. An fMRI study in healthy adults (Anderson et al 2003) found distinct olfactory regions to be involved in orthogonal representations of odor valence (orbitofrontal) and odor intensity (amygdala):



However, there has been relatively little study of olfactory function in depressed patients and existing studies have been limited by lack of neurophysiologic measures and methodological difficulties (cf. Pause et al 2003).

The dependency of surface potentials on a recording reference location (e.g., nose, linked mastoids, average) and the definition and measurement of appropriate ERP components (e.g., specific time windows for peak or integral amplitudes) are two recurring problems in ERP research, which crucially affect component interpretation (e.g., polarity, topography, generator) and statistical analysis (e.g., Kayser & Tenke 2003; Tenke & Kayser 2005). These limitations can be overcome by combining reference-free current source density (CSD) transformations and temporal principal components analysis (PCA) to identify relevant, data-driven components (Kayser & Tenke 2006a,b).

Objective:

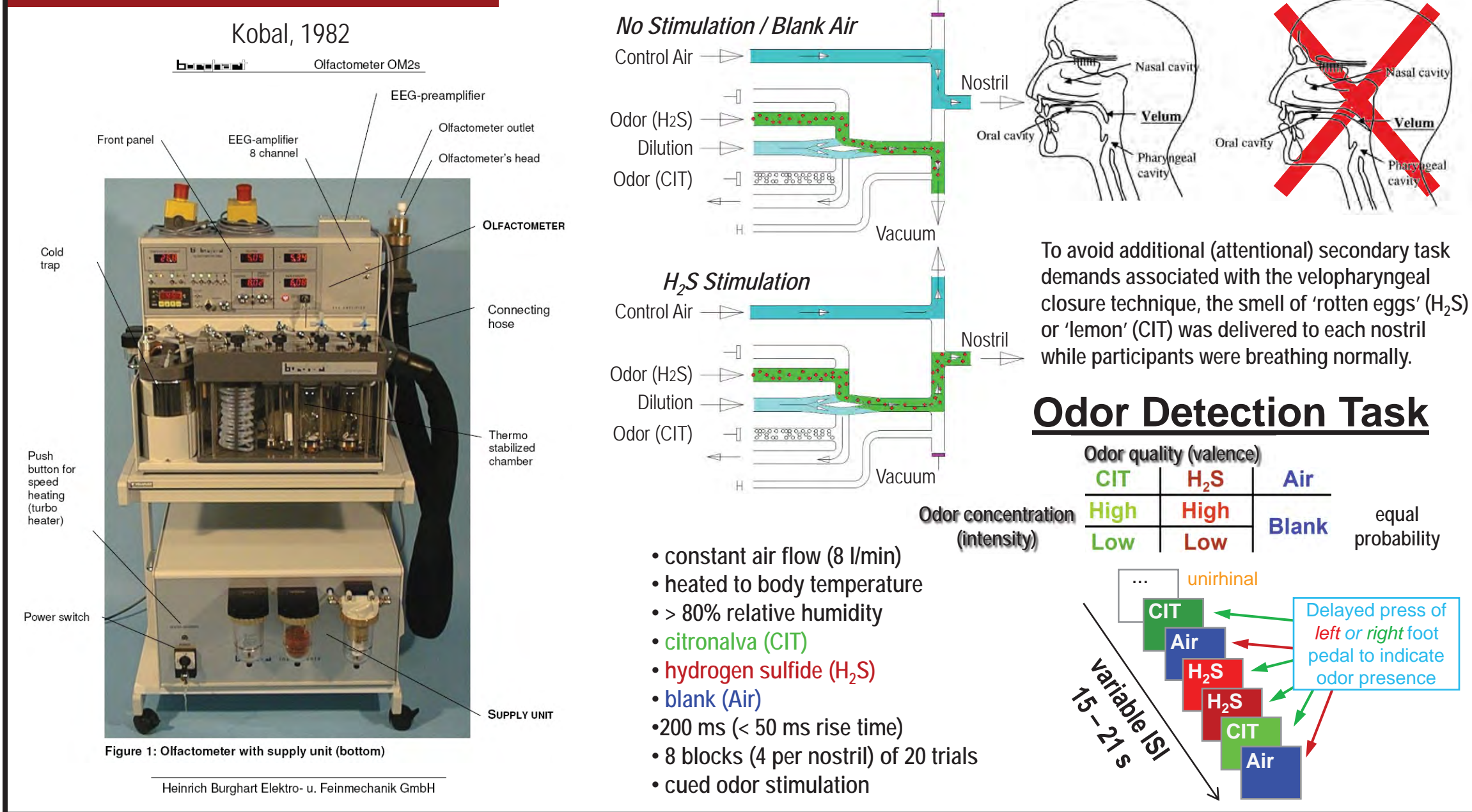
- replicate independent valence-by-intensity odor manipulation of Anderson et al (2003)
- use CSD-PCA approach to identify neuronal generator patterns underlying olfactory ERPs for pleasant and unpleasant odors in depressed patients and healthy adults

Participants

DSM-IV Criteria	Means, Standard Deviations (SD), and Ranges for Demographic and Clinical Variables						p
	Depressed Patients (n = 25; 11 male; 2 smokers)			Healthy Controls (n = 27; 11 male; 2 smokers)			
Variable	Mean	SD	Range	Mean	SD	Range	
Age (years)	41.4	12.6	19 - 58	34.5	10.8	18 - 62	.045
Education (years)	15.5	1.9	11 - 19	15.4	1.9	12 - 21	
Handedness (LQ) *	82.9	34.2	-53 - 100	82.5	23.6	0 - 100	
Medication Status							<.001
Unmedicated > 14 days	BDI ^b	22.5	8.2	8 - 36	0.7	1.7	

* Laterality quotient (Oldfield 1971) can vary between -100.0 (completely left-handed) and +100.0 (completely right-handed)
***** Beck Depression Inventory (Beck et al 1961)
***** no history of any psychopathology or neurology disorder

Stimuli and Procedure



Odor Ratings

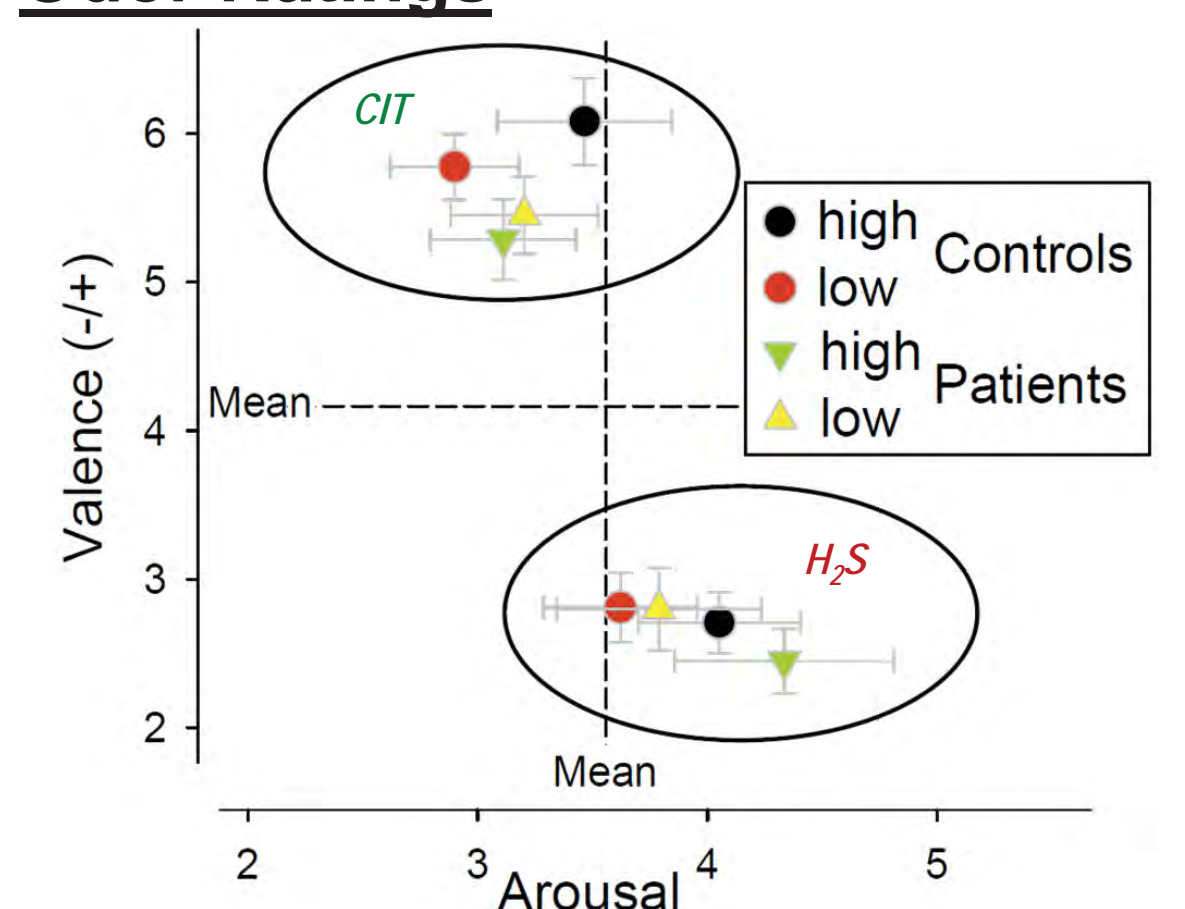


Fig. 1. Mean (SEM) valence and arousal ratings (Likert scale 1-9; pooled across nostrils) for healthy controls and depressed patients. Whereas both groups rated CIT as pleasant and H₂S as unpleasant, H₂S stimuli were also rated as more arousing than CIT stimuli. However, for each odor, high intensity stimuli were rated as more arousing than low intensity stimuli.

Behavioral Data

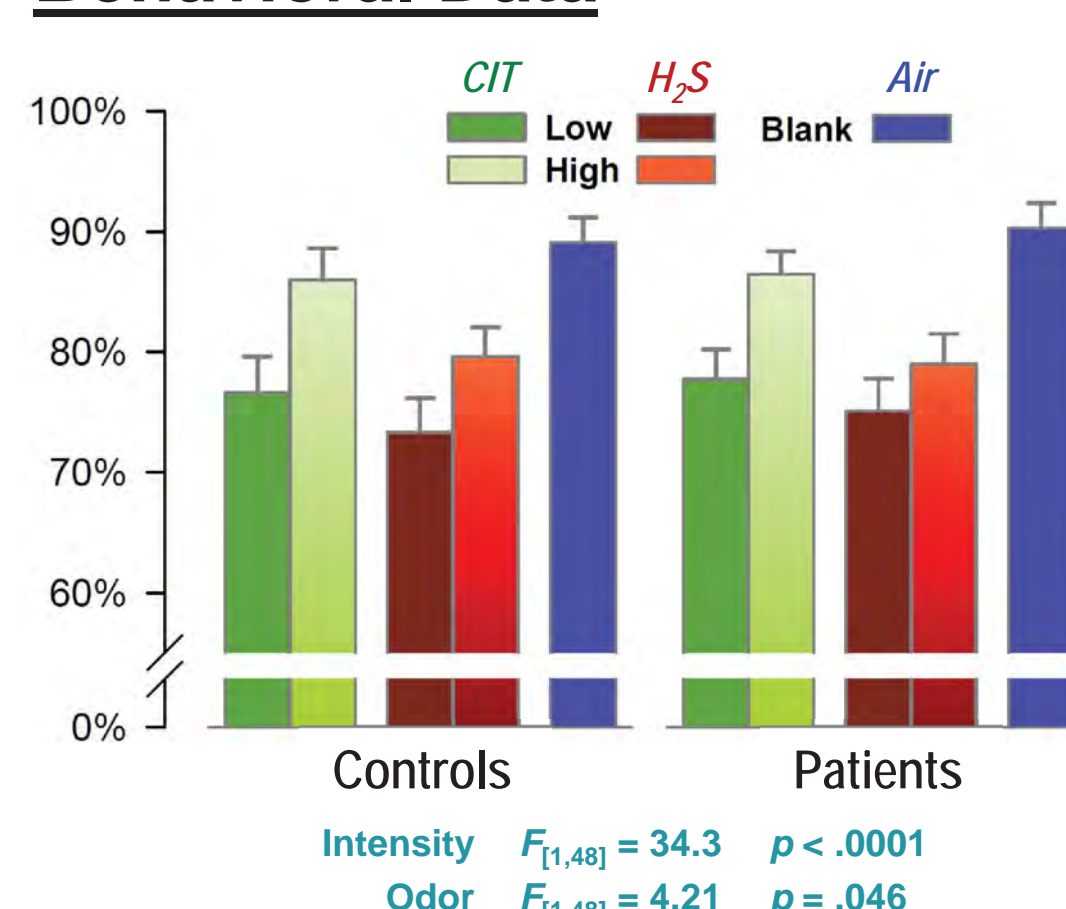


Fig. 2. Mean (SEM) percentage of correct responses (pooled across nostrils) revealed equal performance for healthy controls and depressed patients. Across groups, high intensity odors were more often correctly perceived than low intensity odors. CIT revealed a slightly better performance than H₂S.

Sniffin' Sticks

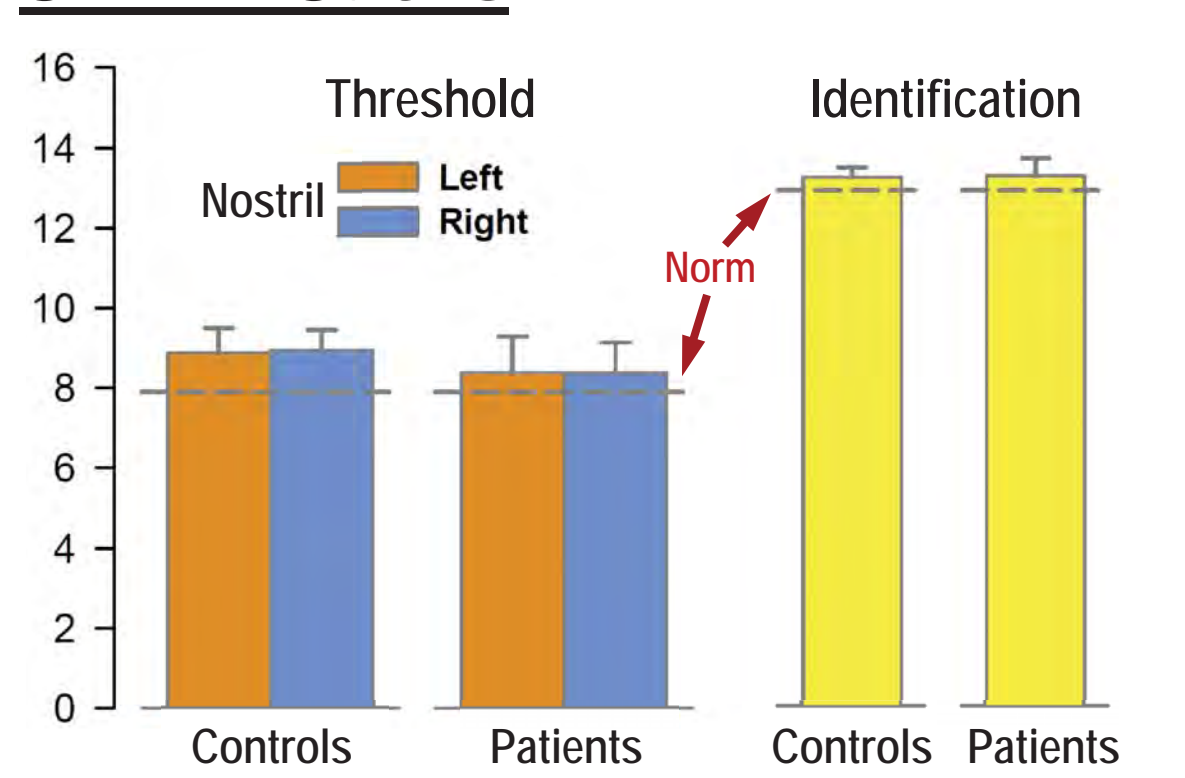


Fig. 3. Nasal chemosensory performance (Sniffin' Sticks; Kobal et al 2000) revealed normal scores of left and right nostril odor thresholds and odor identification for healthy controls and depressed patients.

ERP Recording and Data Analysis

ERPs recorded from 49 scalp placements using an electrode cap with a nose reference, 200 samples/s. EEG data acquired at .01-30 Hz band pass (-6dB/octave). **blink reduction** (continuous EEG) using spatial SVD; interpolated bipolar horizontal and vertical EOGs; horizontal eye artifacts (epoch EEG) by linear regressions of lateral EEG differences (Fp2-Fp1, etc.). **2,000 ms epochs** (250 ms pre-stimulus), averages (artifact-free trials) low pass filtered at 12.5 Hz (-24dB/oct.), 100 ms baseline correction. ERPs re-referenced to linked mastoids (TP9/10) for comparability to previous OERP research and **reference-free current source densities (CSD)** (spherical splines surface Laplacian; Perrin et al 1989) computed for each ERP (sharpen topographies, eliminate volume-conducted activity). data were **pooled across nostrils** because of their blocked presentation order and to obtain more stable ERP/CSD waveforms (i.e., to improve the overall signal-to-noise ratio). **CSDs** submitted to **unrestricted temporal principal components analysis (PCA)** derived from the covariance matrix [401 variables = stimulus-locked samples ~250 to 1,750 ms; 12,740 observations = Subjects (52) x Electrode Sites (49) x Conditions (5)], followed by Varimax rotation of covariance loadings (Kayser & Tenke, 2003, 2006a,b). **PCA #1:** eliminate "noise" factors and reassemble "filtered" CSD waveforms (cf. Tenke et al 2011). **PCA #2:** identify and measure neuronal generator patterns underlying olfactory ERPs from meaningful, high-variance CSD factors corresponding to N1/P2 sinks and sources (submit factor scores to **repeated measures ANOVA** with **group** (patients, controls) and **gender** (male, female) as between-subjects factors, and odor **quality** (H₂S, CIT) and **intensity** (high, low) as a within-subjects factor (**hemisphere** and **site** to reflect CSD topography).

Surface Potentials

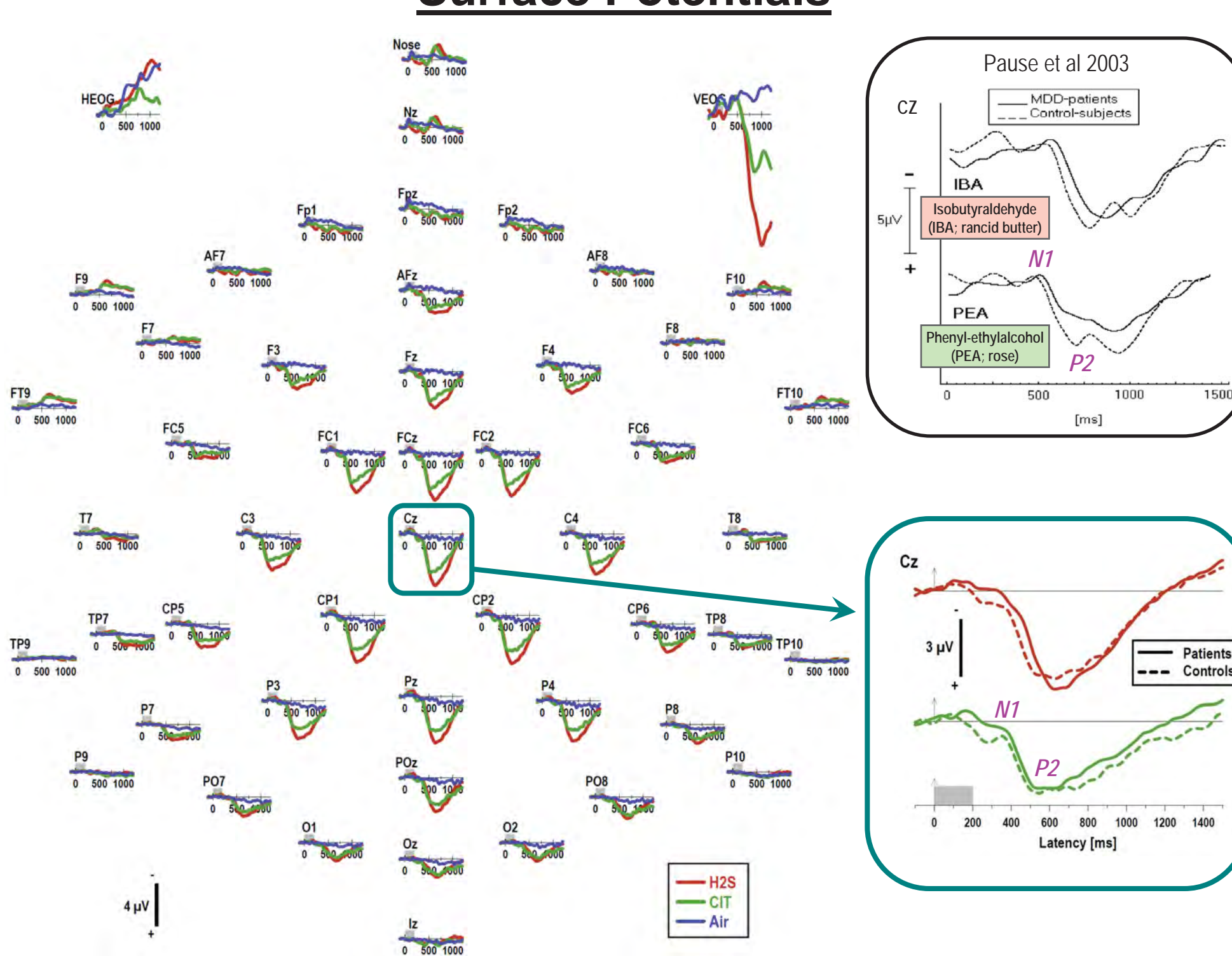


Fig. 4. Grand average OERP waveforms for H₂S and CIT stimuli (pooled across intensity and groups) and blank Air at all 49 sites using a linked-mastoids reference (TP9/10). Prominent deflections at about 350 ms (N1) and 600 ms (P2) at vertex (Cz) are comparable to previous OERP findings using similar odors of negative (IBA) and positive (PEA) valence (Pause et al 2003).

CSD-PCA Factor Loadings

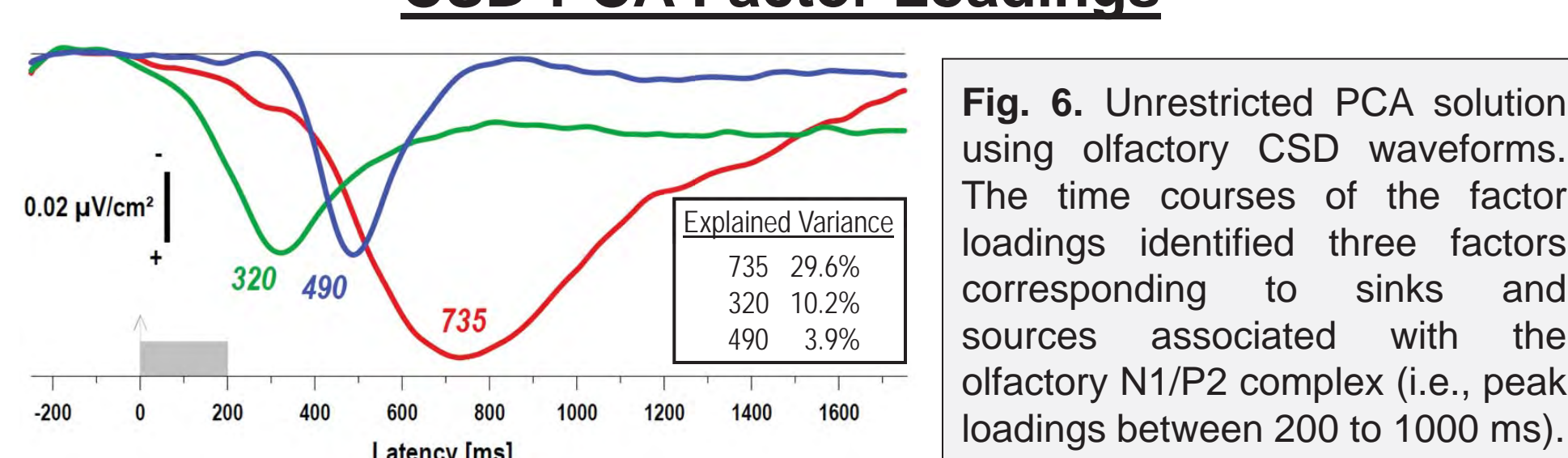


Fig. 6. Unrestricted PCA solution using olfactory CSD waveforms. The time courses of the factor loadings identified three factors corresponding to sinks and sources associated with the olfactory N1/P2 complex (i.e., peak loadings between 200 to 1000 ms).

CSD Waveforms

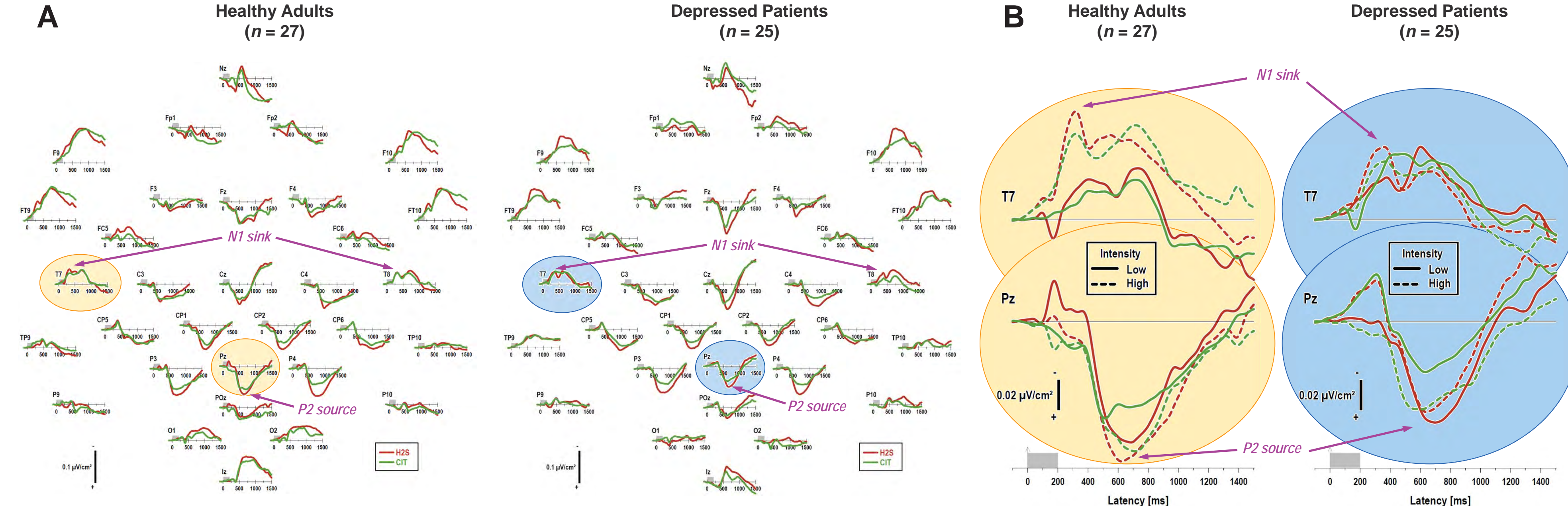


Fig. 5. Grand mean, PCA-filtered CSDs for controls and patients comparing H₂S and CIT stimuli at 32 selected sites (A) and at sites T7 and Pz also comparing odor intensity (B). A) Across odor quality and groups, CSD waveforms revealed distinct bilateral fronto-temporal N1 sinks (approximate peak latencies 315 ms at T7) and mid-parietal P2 sources (620 ms at Pz), which were accompanied by frontolateral sinks. B) Compared to healthy adults, N1 sinks and P2 source appeared to be reduced in depressed patients, particularly for high intensity stimuli.

CSD-PCA Factor Score Topographies

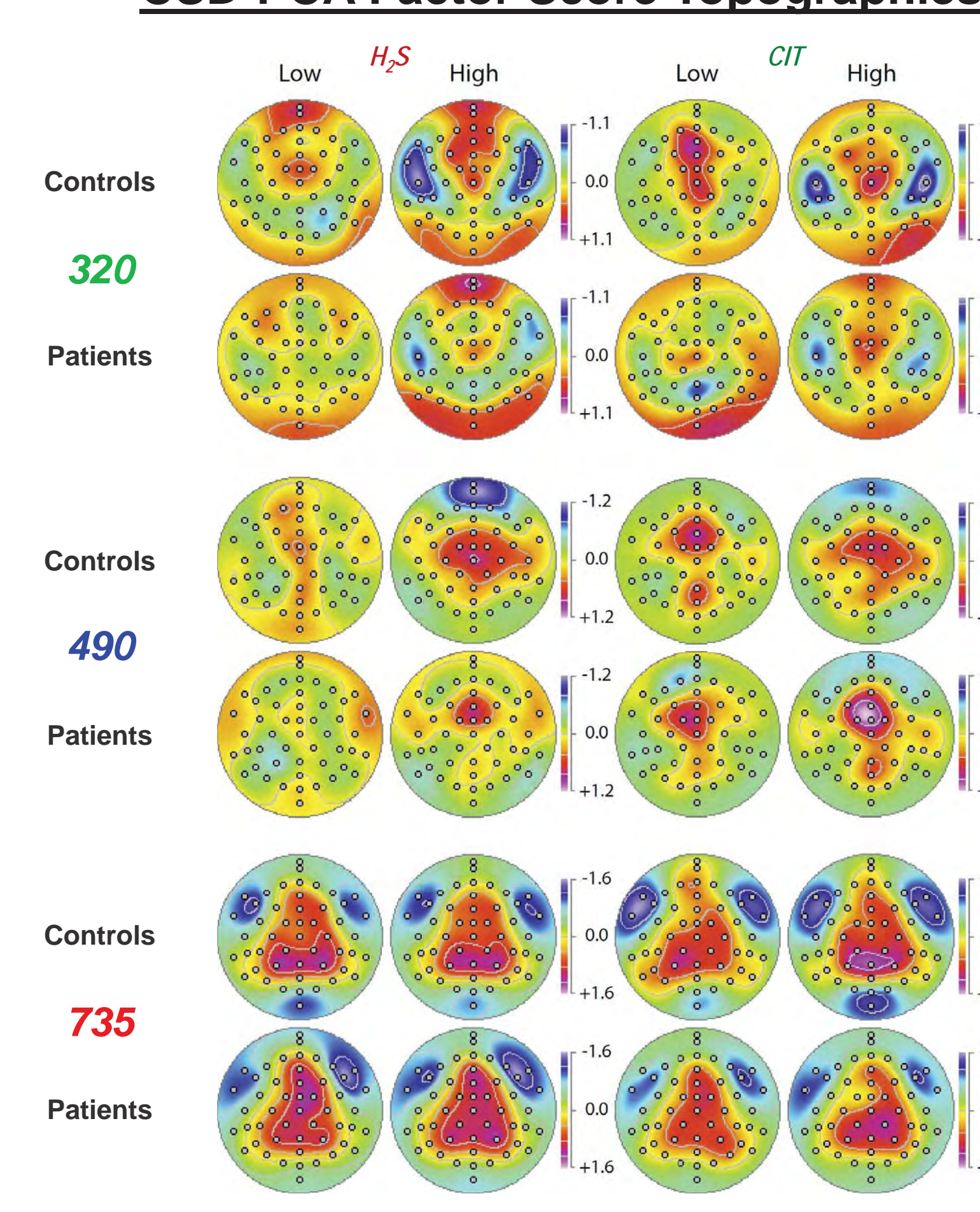
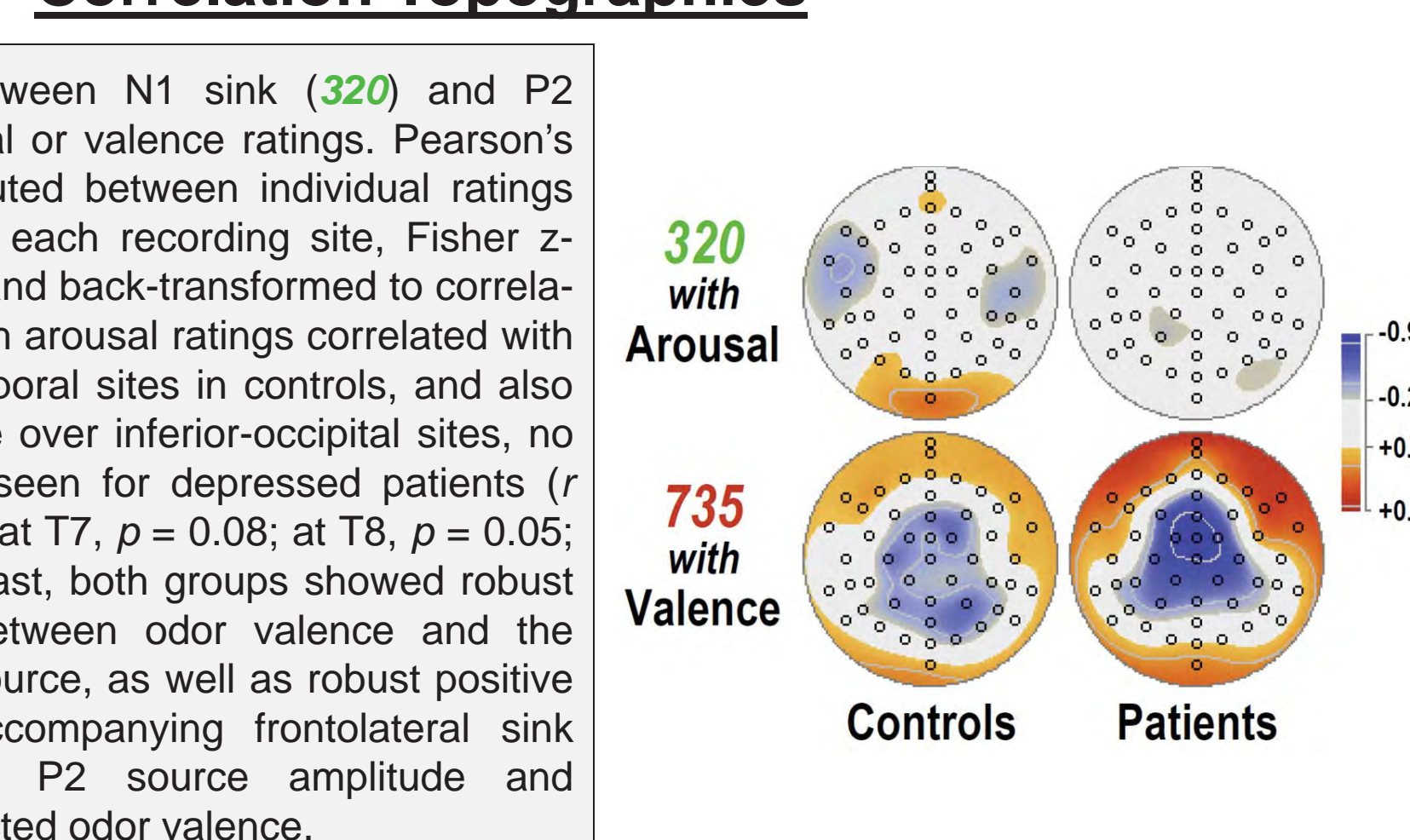


Fig. 7. Factor score topographies for healthy adults and depressed patients comparing unpleasant (H₂S) and pleasant (CIT) odors of low and high intensity. Whereas N1 sink (320) and the mid-frontal source (490) varied with odor intensity, P2 source (735) varied with odor quality (H₂S > CIT).

Correlation Topographies



Summary and Conclusions

- Depressed patients and healthy controls produced highly comparable odor ratings, detection performance, nasal chemosensory performance, and ERP/CSD waveforms/topographies.
- CSD component structure and topography were highly comparable for unpleasant (H₂S) and pleasant (CIT) odors, replicating intensity-dependent bilateral frontotemporal N1 sinks (~300 ms) and mid-parietal P2 sources (~700 ms) previously observed for H₂S stimuli (Kayser et al 2010).
- A completely new finding is the close association of CSD amplitudes and topographies with individual ratings of odor valence and arousal, suggesting distinct processes.
- The dissociation of N1 sink and arousal in depressed patients is in partial agreement with the hypothesis of Pause et al (2003) that odor perception in depression is abnormal on an "early sensory" level.
- The findings do not provide evidence of an abnormal affective evaluation of pleasant (CIT) and unpleasant (H₂S) odors or impaired olfactory ERPs to emotional stimuli in depression.
- However, the independent manipulation of valence and arousal dimensions using pleasant and unpleasant odors did not achieve fully orthogonal ratings as reported by Anderson et al (2003).