Effects of Odor Valence and Arousal on Event-Related Potentials (ERPs) in Healthy Adults and Depressed Patients

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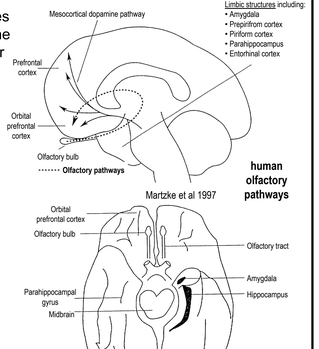
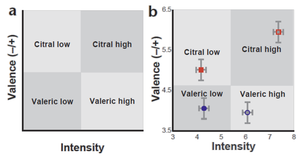
Abstract

Background: Despite the overlap of cortical and limbic structures involved in olfaction, emotion and depression, there has been little study of olfactory function in depression. **Methods**: 49-channel ERPs were recorded from 25 clinically-depressed and 27 healthy controls during an odor detection task using pleasant (Citronalva; CIT) and unpleasant (hydrogen sulfide; H_2S) stimuli. High or low odor concentrations or blank air were presented unilaterally by a constant-flow olfactometer (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**: Replicating previous findings for H_2S stimuli (Kayser et al 2010), CSD waveforms were characterized across odors by an early N1 sink (320 ms, bilateral centrotemporal) and a late P2 source (735 ms, mid-centroparietal). Whereas N1 sink varied with odor intensity, P2 source varied with odor valence (H_2S > CIT). CSD amplitude and topography were highly correlated with individual ratings of valence (P2) in both groups but arousal (N1) in controls only. However, CSD waveforms and topographies did not differ between groups. Likewise, depressed patients showed normal odor identification and thresholds (Sniffin' Sticks), and did not differ from controls in detection accuracy for all conditions (76-90% vs. 74-91% correct). **Conclusions**: Although ERP/CSD measures directly reflected valence and arousal properties of pleasant and unpleasant odors, there was no evidence of impaired olfactory/emotional processing in depression. However, the dissociation of N1 amplitude and arousal ratings in patients may suggest abnormal odor perception on an "early sensory" level 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** (Anderson et al 2003)
- **use CSD-PCA approach to identify and quantify neuronal generator patterns underlying olfactory ERPs for pleasant and unpleasant odors**
- **if depressed patients have a deficit in responding to odorants differing in valence and intensity, this should be reflected in reduced oERP components compared with healthy adults**

Participants

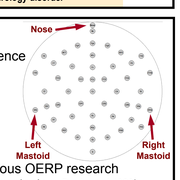
Means, Standard Deviations (SD), and Ranges for Demographic and Clinical Variables

		Depressed Patients (*n* = 25; 11 male; 2 smokers)			Healthy Controls (*n* = 27; 11 male; 2 smokers)			
DSM-IV Criteria	Variable	Mean	SD	Range	Mean	SD	Range	*p*
MDD (*n* = 11)	Age (years)	41.4	12.6	19 - 58	34.5	10.8	18 - 62	.045
Dysthymia (*n* = 8)	Education (years)	15.5	1.9	11 - 19	15.4	1.9	12 - 21	
MDD + Dyst. (*n* = 6)	Handedness (LQ) [a]	82.9	34.2	-53 - 100	82.5	23.6	0 - 100	
Medication Status	BDI [b]	22.5	8.2	8 - 36	0.7	1.7	0 - 8	<.001
Unmedicated > 14 days								

[a] Laterality quotient (Oldfield 1971) can vary between -100.0 (completely left-handed) and +100.0 (completely right-handed)
[b] Beck Depression Inventory (Beck et al 1961)

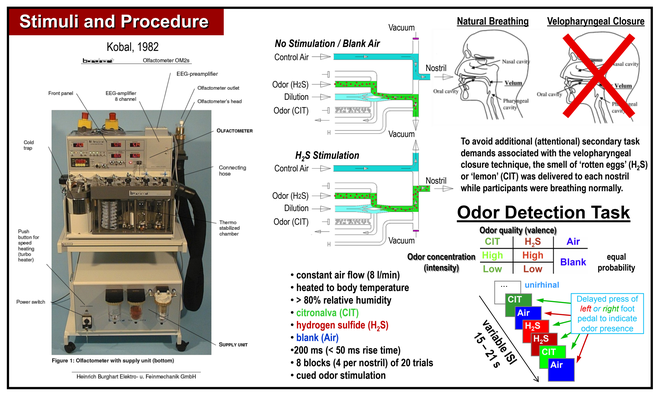
• no history of any psychopathology or neurology disorder

ERP Recording and Data Analysis

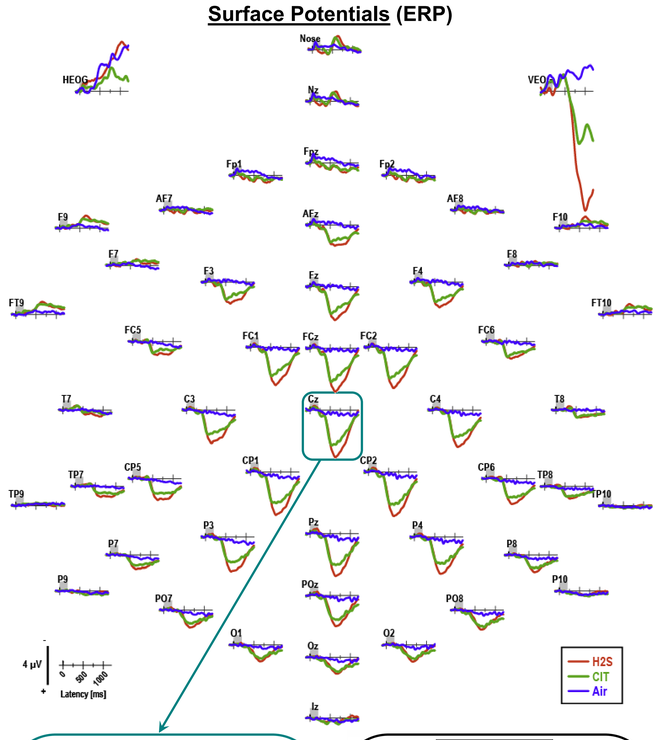


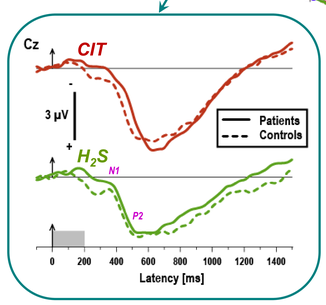
- ERPs recorded from 49 scalp sites using an electrode cap with a nose reference
- EEG data acquired at .01-30 Hz band pass (-6dB/octave), 200 samples/s
- **blink reduction** (continuous EEG) **using spatial SVD**; interpolated bipolar horizontal and vertical EOGs; horizontal eye artifacts (epoched EEG) 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
- **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)** [401 variables = stimulus-locked samples –250 to 1,750 ms; 12,740 observations = 52 *Subjects* x 49 *Recording Sites* x 5 *Conditions*], 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* (H_2S, *CIT*) and *intensity* (high, low) as a within-subjects factor (*hemisphere* and *site* to reflect CSD topography)

Stimuli and Procedure



Surface Potentials (ERP)





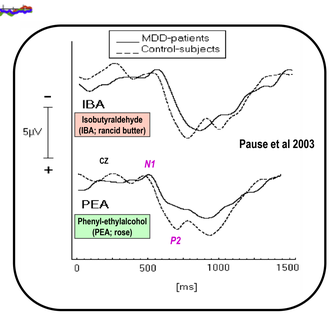


Fig. 4. Grand average OERP waveforms for H_2S and *CIT* stimuli (pooled across intensity and groups) and blank *Air* at all 49 sites using a linked-mastoids reference (TP9/10). Prominent deflections at about 350 ms (*N1*) and 600 ms (*P2*) at vertex (Cz) are comparable to previous OERP findings using similar odors of negative (IBA) and positive (PEA) valence (Pause et al 2003).

Summary and Conclusions

- **Depressed patients and healthy controls produced highly comparable odor ratings** (Fig. 1), **detection performance** (Fig. 2), **nasal chemosensory performance** (Fig. 3), **and ERP/CSD waveforms** (Figs. 4 and 5) **and topographies** (Fig. 7).
- **CSD component structure and topography were highly comparable for unpleasant (H_2S) and pleasant (*CIT*) odors, replicating intensity-dependent bilateral frontotemporal N1 sinks (~300 ms) and mid-parietal P2 sources (~700 ms) previously observed for H_2S 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** (Fig. 8), **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.**
- **In this regard, there was a trend for N1 sink amplitude for high intensity stimuli to be smaller in patients over lateral temporal sites (T7/8) where N1 sink was maximal** (Figs. 5 and 7).
- **The findings do not provide evidence of an abnormal affective evaluation of pleasant (*CIT*) and unpleasant (H_2S) odors or impaired olfactory ERPs to emotional stimuli in depression.**
- **However, this conclusion is limited given that the independent manipulation of valence and arousal dimensions using pleasant and unpleasant odors did not achieve fully orthogonal ratings** (Fig. 1) **as reported by** Anderson et al (2003).

Odor Ratings

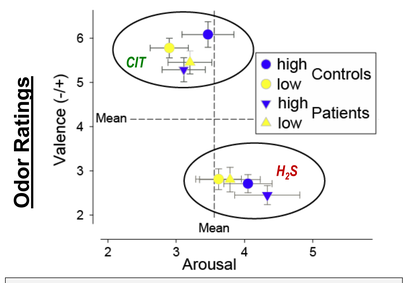


Fig. 1. Mean (SEM) valence and arousal ratings (Likert scale 1-9; pooled across nostrils) for healthy controls and depressed patients. Whereas both groups rated *CIT* as pleasant and H_2S as unpleasant, H_2S stimuli were also rated as more arousing than *CIT* stimuli. However, for each odor, high intensity stimuli were rated as more arousing than low intensity stimuli.

Behavioral Data

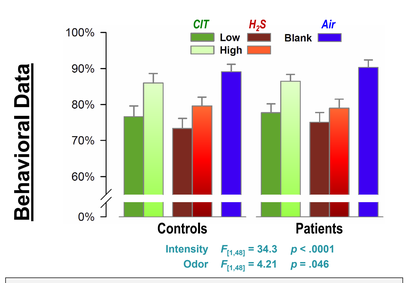


Fig. 2. Mean (SEM) percentage of correct responses (pooled across nostrils) revealed equal performance for healthy controls and depressed patients. Across groups, high intensity odors were more often correctly perceived than low intensity odors. *CIT* revealed a slightly better performance than H_2S.

Sniffin' Sticks

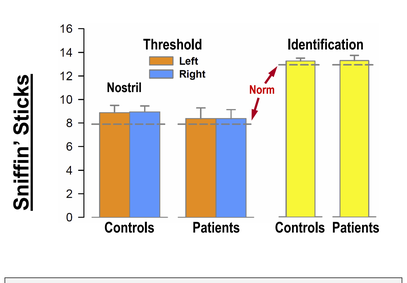


Fig. 3. Nasal chemosensory performance (Sniffin' Sticks; Kobal et al 2000) revealed normal scores of left and right nostril odor thresholds and odor identification for healthy controls and depressed patients.

Current Source Densities (CSD)

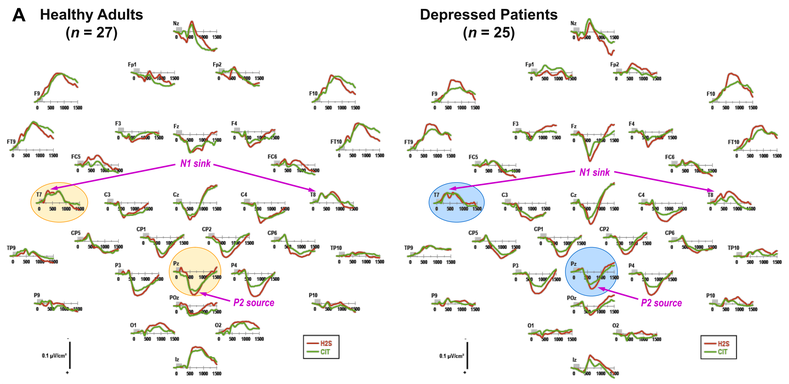


Fig. 5. Grand mean, PCA-filtered CSDs for controls and patients comparing H_2S and *CIT* stimuli at 32 selected sites **(A)** and at sites T7 and Pz also comparing odor intensity **(B)**.

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 Loadings

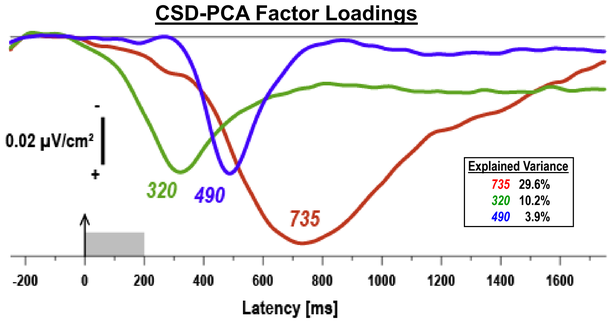


Fig. 6. Unrestricted PCA solution using olfactory CSD waveforms. The time courses of the factor loadings identified three factors corresponding to sinks and sources associated with the olfactory N1/P2 complex (i.e., peak loadings between 200 to 1000 ms).

Correlation Topographies

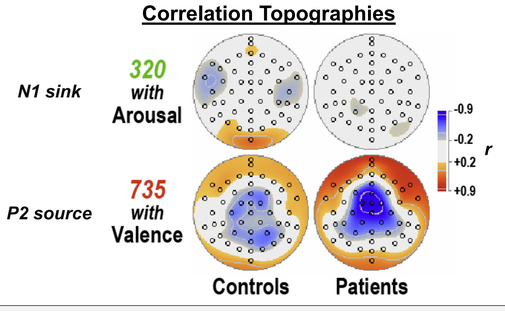


Fig. 8. Association between N1 sink (*320*) and P2 source (*735*) and arousal or valence ratings. Pearson's correlations were computed between individual ratings and CSD amplitudes at each recording site, Fisher z-transformed, averaged, and back-transformed to correlation coefficients. Although arousal ratings correlated with N1 sink over lateral-temporal sites in controls, and also its accompanying source over inferior-occipital sites, no such correlations were seen for depressed patients (r differed between groups at T7, p = 0.08; at T8, p = 0.05; at Iz, p = 0.01). In contrast, both groups showed robust negative correlations between odor valence and the broadly distributed P2 source, as well as robust positive correlations with its accompanying frontolateral sink activity, indicating that P2 source amplitude and topography directly reflected odor valence.

CSD-PCA Factor Score Topographies

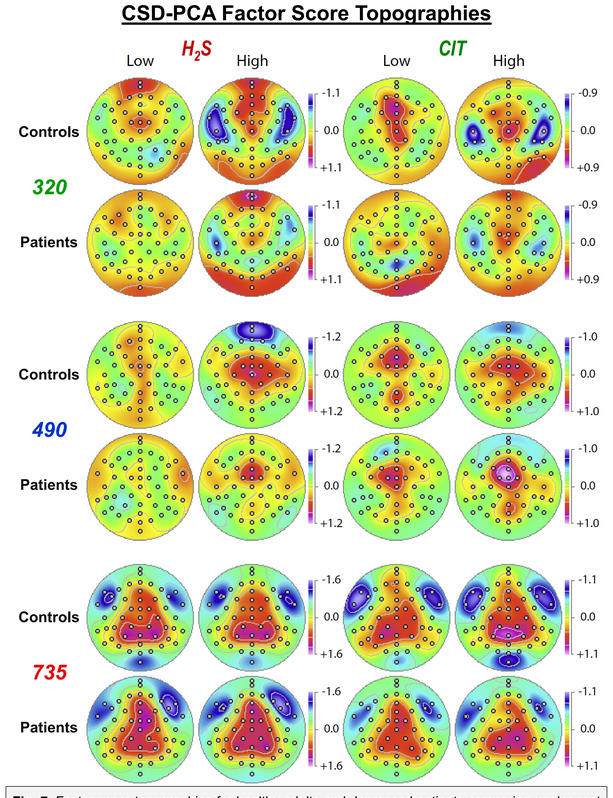


Fig. 7. Factor score topographies for healthy adults and depressed patients comparing unpleasant (H_2S) and pleasant (*CIT*) odors of low and high intensity. Whereas N1 sink (*320*) and the mid-frontal source (*490*) varied with odor intensity, P2 source (*735*) varied with odor quality (H_2S > *CIT*). There was a trend for reduced N1 sinks at lateral temporal sites (T7/8) for high intensity stimuli in depressed patients (Group x Intensity, $F_{[1,48]}$ = 3.05, p = .09).

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