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Identifying Generators of Visual Recognition Memory (Old/New) Effects in Affective Disorders: A Principal Components Analysis (PCA) of Laplacian Waveforms

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Jürgen Kayser[1,3], Craig E. Tenke[1,3], Nathan A. Gates[1], Chris J. Kroppman[1], James P. Sedoruk, Carlye B. Griggs, Jonathan W. Stewart[2,3], Frederic M. Quitkin[2,3], Gerard E. Bruder[1,3]

[1] Department of Biopsychology and [2] Depresssion Evaluation Service, New York State Psychiatric Institute, New York, NY; [3] Department of Psychiatry, College of Physicians and Surgeans, Columbia University, New York, NY

Abstract

Event-related potential (ERP) correlates of mnemonic processes have rarely been assessed in mood disorders, despite considerable behavioral evidence of impairment. The typical ERP finding for healthy adults during explicit memory tasks is the so-called 'old/new effect,' an enhanced posterior positivity between 300 and 800 ms for repeated items, which is assumed to index conscious recollection. This study compared 67-channel, reference-free current source densities (CSD; Laplacian) derived from surface potential ERPs recorded during visual recognition memory tasks using unknown faces (college yearbook) and pronouncable pseudo-words (e.g., 'cernor') from 30 unmedicated outpatients (major depressive disorder or dysthymia, DSM-IV) and 30 healthy adults, all right-handed. Patients performed more poorly than controls, with both groups having better memory for faces than pseudo-words. Unrestricted principal components (Varimax) were derived from CSD waveforms to identify and measure neuronal generator patterns. Two prominent CSD factors, related to current sources at parietal and temporal sites, revealed old/new effects at mid-frontal (422 ms peak latency) and inferior-parietal sites (809 ms). These sources and their old/new effects were reduced in patients at parietal and mid-central sites, especially for faces. Task-specific CSD topographies (< 300 ms) were comparable across groups, dissociating neuronal generators of early word and face processing. The combination of PCA and CSD methodologies can help to identify neuronal generators underlying memory impairments in depression.

Introduction

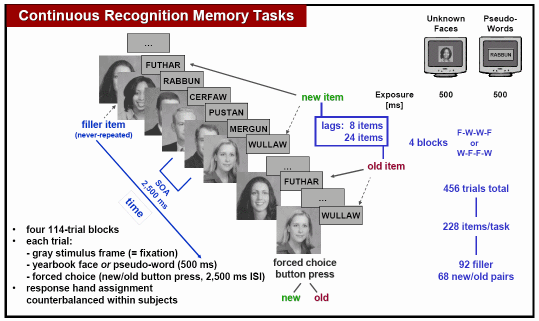
- **In addition to disturbances in mood, depressed patients often also show cognitive deficits, including memory functions, which may result from medial-temporal and frontal dysfunction (e.g., Heller & Nitschke, 1997).**
- **Surprisingly, few studies have directly measured neurophysiologic function of depressed patients during memory tasks (e.g., Dietrich et al., 2000), although the fine temporal resolution and scalp topography of event-related brain potentials (ERPs) reflect the spatiotemporal sequence of cortical information processing.**
- **Typical ERP finding during explicit memory-retrieval tasks (judging items as *old* or *new*) is the *Old-New Effect*:**
  - **begins at 200 – 400 ms, lasts 300 – 500 ms (or longer), more positive to *old***
  - **overlaps at least two distinct ERP components: *N400/N2* and *P600/P3b***
  - **scalp distribution differs from *N2* and *P3* topographies**
  - **mostly posterior parietal (conscious recollection, *P600*)**
  - **also mid-frontal (item familiarity, *FN400*; e.g., Curran, 1999)**
  - **words, pictures, faces, etc.**

Objective: Compare ERP old-new effects in affective disorders using linguistic and face stimuli

Participants

	Healthy Adults (n = 30)		Depressed Patients (n = 30)
	• no history of any psychopathology or neurology disorder • matched to patients for core demographics (only approximation for age)		• unmedicated outpatients • DSM-IV - *major depressive disorder (n = 14)* - *dysthymic disorder (n = 7)* - *MDD + dysthymic disorder (n = 9)*
Gender (male/female)	13 / 17		14 / 16
Age (years)	28.8 ± 9.1 (19 – 55)	p = .003	37.2 ± 11.5 (22 – 63)
Education (years)	15.4 ± 2.5 (12 – 20)		15.3 ± 2.3 (6 – 18)
Handedness (EHI)	80.7 ± 24.3 (0.0 – 100.0)		75.1 ± 23.9 (25.0 – 100.0)
Beck Depression Inventory (BDI)	1.3 ± 1.8 (0 – 7)	p < .0001	22.0 ± 7.4 (8 – 41)

Continuous Recognition Memory Tasks



- four 114-trial blocks
- each trial:
  - gray stimulus frame (= fixation)
  - yearbook face or pseudo-word (500 ms)
  - forced choice (new/old button press, 2,500 ms ISI)
- response hand assignment counterbalanced within subjects

ERP Recording and Data Analysis

- Continuous DC (24-bit A/D) EEGs using an electrode cap, 67 scalp sites (extended 10-20 system), active recording reference (BioSemi), 256 samples/s
- Bipolar horizontal and vertical EOGs; **blink reduction** (continuous EEG) **using spatial SVD**; horizontal eye artifacts (epoched EEG) by linear regressions of lateral EEG differences (Fp2-Fp1, etc.)
- **2,000 ms epochs**, 300 ms pre-stimulus baseline, ERP averages (artifact-free trials, correct responses only) low pass filtered at 12.5 Hz (-24dB/oct.), 100 ms baseline correction
- **reference-free current source densities** (CSD; spherical splines surface Laplacian; Perrin et al., 1989, 1990) computed for each ERP (sharpen topographies, eliminate volume-conducted activity from distant regions)
- CSDs submitted to ***unrestricted* temporal principal components analysis (PCA)** derived from the covariance matrix [409 variables = samples –100 to 1,492 ms; 16,080 observations = *Subjects* (60) x *Electrode Sites* (67) x *Condition* (new/old) x *Task* (face/word)], followed by *unscaled* Varimax rotation (Kayser & Tenke, 2003, in press a,b), to identify and measure neuronal generator patterns
- ***CSD data*:** Meaningful PCA components spanning time interval (300 ... 1,200 ms) of targeted old-new effects; 1) topographic differences of factor scores evaluated by randomization distribution of *HotellingsT²* statistics (pooled variance using all conditions) for old/new effects (dependent) and group differences (independent; Maris, 2004); 2) factor scores at representative recording sites submitted to repeated measures ANOVA with *Group* (patients, controls), *Gender* (male/female), *Condition* (new/old), *Task* (face/word), and *Site/Hemisphere* as between- and within-subjects factors
- ***Behavioral data*:** Percentage of correct responses, sensitivity (*dL*), and mean response latency of correct responses submitted to repeated measures ANOVA with *Group* (patients, controls), *Gender* (male/female), *Condition* (new/old), and *Task* (face/word) as between- and within-subjects factors

Current Source Densities

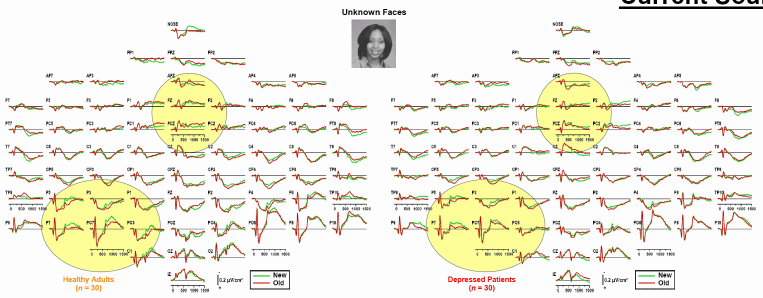


Fig. 2. Reference-free current source density (CSD) [μV/cm²] waveforms (spherical spline Laplacians; Perrin et al., 1989, 1990) to unknown yearbook faces for 30 healthy adults (left panel) and 30 depressed patients (right panel) comparing old and new stimuli at all 67 recording sites. Stimulus-specific CSD components were well-defined over the posterior scalp, including a prominent source-sink-source (P1-N1-P2) complex over right inferior parieto-occipital sites (e.g., PO8). Old-new effects (> 300 ms) are evident over various regions, including mid-frontal (e.g., FCz) and left posterior scalp sites (e.g, P5, P3, P7, PO7), and appear to be reduced in patients (see shaded areas).

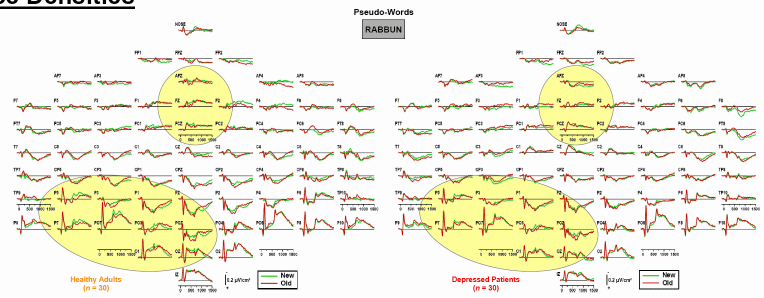
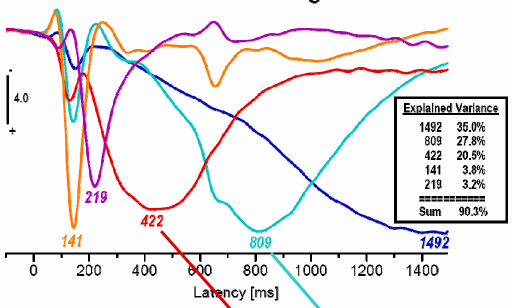


Fig. 3. Reference-free current source density (CSD) [μV/cm²] waveforms (spherical spline Laplacians; Perrin et al., 1989, 1990) to pseudo-words for 30 healthy adults (left panel) and 30 depressed patients (right panel) comparing old and new stimuli at all 67 recording sites. Stimulus-specific CSD components were largely comparable to those for faces, that is, well-defined over the posterior scalp. Old-new effects (> 300 ms) are also evident over various regions, including mid-frontal (e.g., AFz, Fz) and left-medial posterior scalp sites (e.g, P5, P3, P7, PO7, PO3, PO2), and again reduced in depressed patients compared to healthy adults.

PCA Factor Loadings



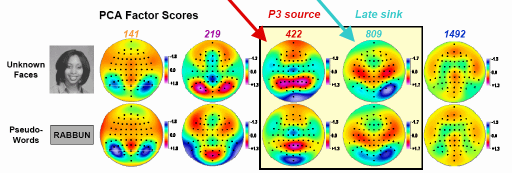


Fig. 4. Time courses and percentage of explained variance of Varimax-rotated covariance loadings for the first five PCA components, and corresponding factor score topographies of task means (pooled across group and condition). CSD factors *422* and *809* were selected for further analysis.

Behavioral Data

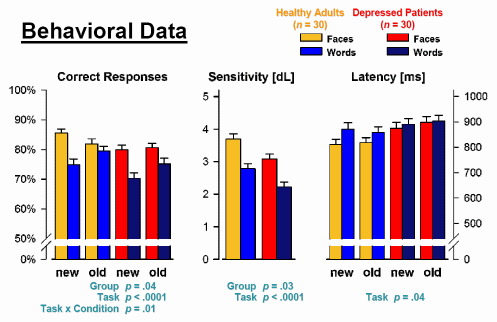


Fig. 1. Mean (SEM) percentage of correct responses, sensitivity, and response latency for healthy adults and depressed patients comparing yearbook faces and pseudo-words. Recognition memory for pseudo-words was the more difficult task. Depressed patients showed poorer recognition memory than controls across tasks.

Topographies of PCA Factor Scores

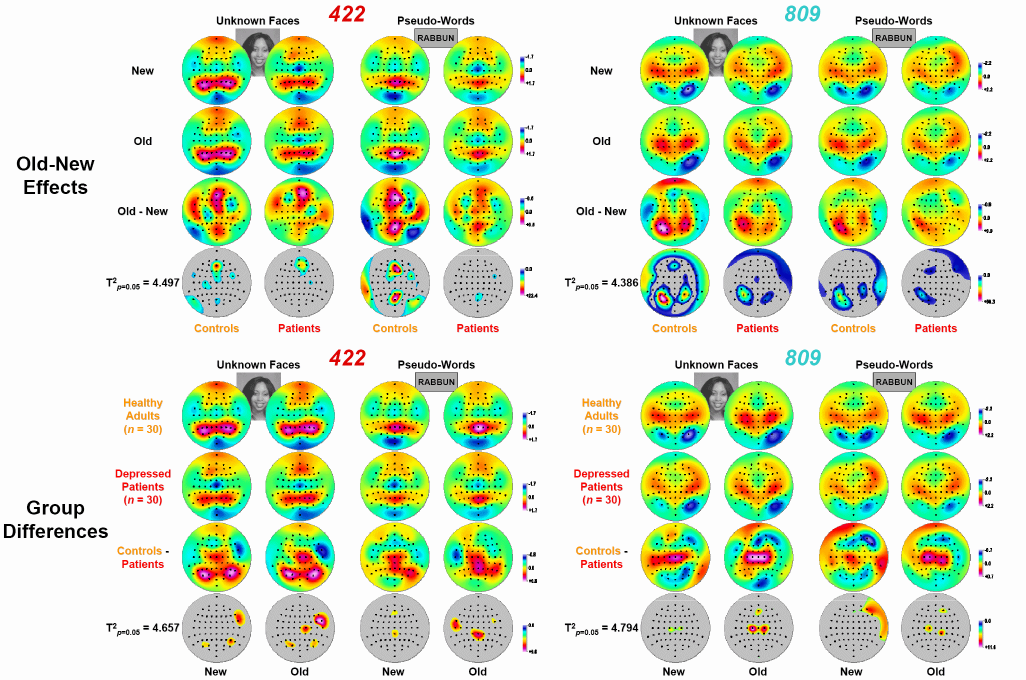


Fig. 5. Mean topographies of factor scores for PCA components extracted from CSD waveforms for 30 healthy adults and 30 depressed patients. Topographies of *Hotellings T²* values are plotted using a randomization distribution with a p=0.05 significance threshold (bottom rows) to evaluate old-new effects (top panels) and group differences (bottom panels) for CSD factors *422* (left panels) and *809* (right panels) in both tasks.

References

Curran T (1999). The electrophysiology of incidental and intentional retrieval: ERP old/new effects in lexical decision and recognition memory. Neuropsychologia 37(7):771-785.

Dietrich DE, Emrich HM, Waller C, Weringa BM, Johannes S, Munte TF (2000). Emotion/cognition-coupling in word recognition memory of depressive patients: an event-related potential study. Psychiatry Res. 98(1):15-29.

Heller W, Nitschke JB (1997). Regional brain activity in emotion: a framework for understanding cognition in depression. Cogn. Emot. 11(5-6):637-661.

Kayser J, Tenke CE (2003). Optimizing PCA methodology for ERP component identification and measurement: theoretical rationale and empirical evaluation. *Clin. Neurophysiol.* 114(12):2307-2325.

Kayser J, Tenke CE (in press, a). Principal components analysis of Laplacian waveforms as a generic method for identifying ERP generator patterns: I. Evaluation with auditory oddball tasks. *Clin. Neurophysiol.*

Kayser J, Tenke CE (in press, b). Principal components analysis of Laplacian waveforms as a generic method for identifying ERP generator patterns: II. Adequacy of low-density estimates. *Clin. Neurophysiol.*

Perrin F, Pernier J, Bertrand O, Echallier JF (1989). Spherical splines for scalp potential and current density mapping [1990 Corrigenda EEG 02274, *Electroenceph. Clin. Neurophysiol.*76:565]. *Electroencephalogr. Clin. Neurophysiol.* 72(2):184-187.

Maris E (2004). Randomization tests for ERP topographies and whole spatiotemporal data matrices. Psychophysiology 41(1):142-151.

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Summary and Conclusions

- **For healthy adults and depressed patients, both recognition memory tasks produced distinct CSD components and topographies, which were concisely summarized by PCA.**
- **Mid-frontal and posterior (reference-free) CSD old-new effects were present in both tasks and both groups, with comparable time courses (400 - 1,200 ms), but more subtle and delayed than previously observed with real word stimuli.**
- **Old-new effects were reduced in depressed patients compared to controls for both unknown faces and pseudo-words, which parallels their poorer recognition memory.**
- **As with old/new effects, topographies of group differences were superimposed on and separable from the observed current generators characteristic of these tasks.**
- **Given the considerable heterogeneity among depressed patients, it will be important to examine the relations of these findings to specific clinical features (treatment response, diagnostic subtype, etc.)**