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Reference-independent ERP old/new effects of auditory and visual word recognition memory: Joint extraction of stimulus- and response-locked neuronal generator patterns

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Abstract

The interpretation of ERPs, which have been used to study episodic memory retrieval, crucially depends on the choice of EEG reference location and on analysis procedures. By contrast, temporal principal components analysis (unrestricted Varimax rotation of covariance loadings) of current source density (CSD) waveforms provides a data-driven, reference-free summary of generator patterns underlying scalp-recorded ERPs. To clarify polarity, topography and time course of recognition memory ERP old/new effects during matched visual and auditory continuous word recognition tasks, unrestricted temporal PCA jointly analyzed stimulus- and response-locked CSDs (31-channel, *N* = 40). Randomization tests provided unbiased statistics for complete factor topographies. Old/new left parietal source effects were complemented by old/new lateral frontocentral sink effects in both modalities, overlapping highly distinct (temporally and topographically) modality-specific P3 sources occurring approximately 160 ms before response onset. A sharp mid-frontal sink 45 ms post-response terminated the frontoparietal generator pattern, showed old/new effects consistent with bilateral activation of anterior cingulate and supplementary motor area, and preceded similar activity extending posteriorly along the longitudinal fissure. These methods separated old/new stimulus source (pre-response) and response sink (post-response) effects from motor and modality-specific ERPs, indicating considerable independence of modality-unspecific old/new effects within a frontal-parietal recognition memory network.

Introduction

- **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*)
  - words, pictures, faces, etc.
- There are, however, **other ERP old/new effects**, including a negative-going posterior potential at or around the time of the subjects' response, which may index different cognitive processes (e.g., item reevaluation, action monitoring). The functional role of this **late episodic memory effect** could be clarified by directly comparing it for **different stimulus modalities** or **by aligning ERPs to response onset** (Friedman et al., 2005; Johansson & Mecklinger, 2003).
- The dependency of surface potentials on a **recording reference location** (e.g., nose, linked mastoids, average; Fig. 2) 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:
- exploit CSD-PCA approach for improved characterization of ERP old/new effects
- employ closely matched auditory and visual continuous word recognition memory tasks
- disentangle shared and unique contributions of stimulus- and response-related processes by joint analysis of stimulus- and response-locked activity using the same *prestimulus* baseline
- avoid experimenter bias in selecting an appropriate analytical design (e.g., which and how many scalp locations to include in what ANOVA model) by using randomization tests

Participants

Healthy Adults (*N* = 40)

- right-handed volunteers
- no history of any psychopathology or neurology disorder
- paid $15/h
- standard audiometric screening / normal or corrected-to-normal vision

Gender (male/female)	19 / 21
Age (years)	28.6 ± 6.8
Education (years)	16.0 ± 2.1
Handedness (EHI)	80.5 ± 22.5

Auditory and Visual Continuous Recognition Memory Tasks

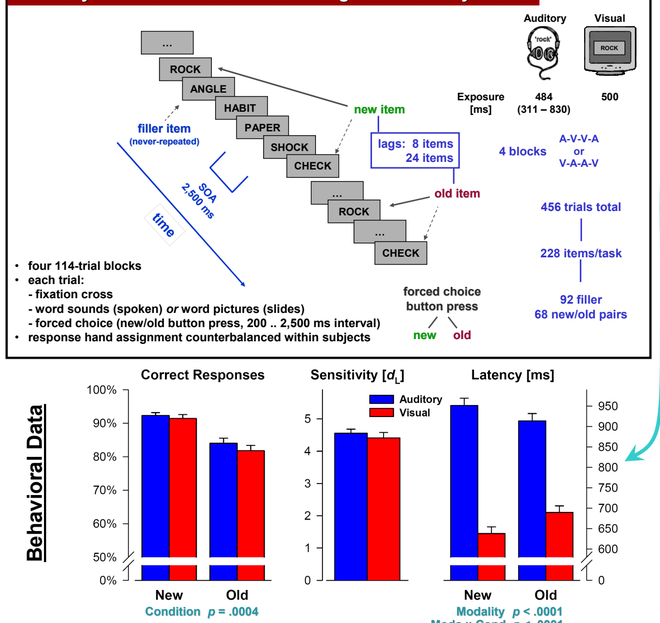
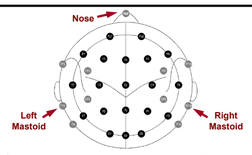


Fig. 1. Mean (SEM) percentage of correct responses, logistic *d'*-like sensitivity measure d_L, and response latency of correct responses revealed good performance for both modalities, however, responses were 200 to 300 ms slower for spoken words.

ERP Recording and Data Analysis



- ERPs recorded from 30 scalp placements using an electrode cap with a nose reference, 200 samples/s
- EEG data acquired at .1-30 Hz band pass (-6dB/octave)
- 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), averages (artifact-free trials, correct responses only) low pass filtered at 12.5 Hz (-24dB/oct.), 100 ms baseline correction = ***stimulus-locked ERPs***
- **1,000 ms subepochs** (700 ms pre-response) derived from stimulus-locked ERPs using the same stimulus-locked baseline (100 ms pre-stimulus) = ***response-locked ERPs***
- **reference-free current source densities (CSD)** (spherical splines surface Laplacian; Perrin et al., 1989) computed for each ERP (sharpen topographies, eliminate volume-conducted activity)
- **concatenated stimulus- and response-locked CSDs** submitted to ***unrestricted* temporal principal components analysis (PCA)** derived from the covariance matrix [601 variables = stimulus-locked samples –300 to 1,695 ms + response-locked samples -700 to 300 ms; 4,960 observations = *Subjects* (40) x *Electrode Sites* (31) x *Condition* (2) x *Lag* (2)] **for each modality**, followed by Varimax rotation of covariance loadings (Kayser & Tenke, 2003, 2006a,b), to identify and measure neuronal generator patterns and their common or unique contributions to stimulus- and/or response-locked activity
- data were pooled across lag to reduce the complexity of the design (there were no meaningful behavioral differences as a function of lag)
- ***Randomization tests***: Old/new effects of meaningful PCA components (topographic differences of factor scores) were statistically evaluated by computing paired samples randomization distributions of scaled multivariate *Hotellings*T^2 statistics (10,000 repetitions) for each CSD factor, followed post-hoc by Scheffé-like paired samples maximum randomization distributions of the univariate (channel-specific) T^2 statistic (Maris, 2004)

Surface Potentials

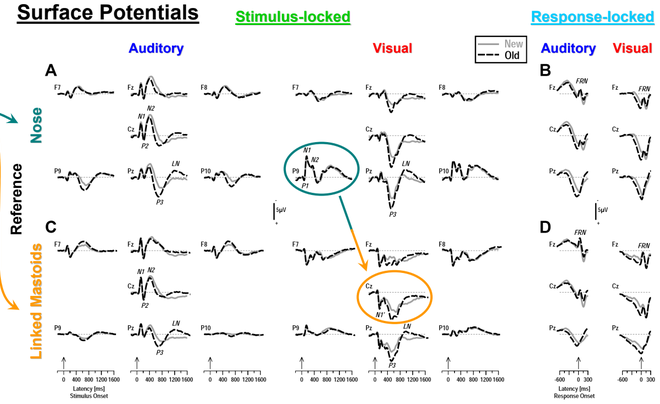


Fig. 2. Stimulus-locked (A, C) and response-locked (B, D) grand average ERP waveforms comparing new and old auditory or visual stimuli at selected sites using a nose tip (A, B) or linked-mastoids reference (C, D). Due to subtracting the mean mastoid activity, stimulus-locked early negative components (e.g., *N1*), which are prominent over inferior-lateral sites for visual stimuli when using a nose reference, are inverted and shifted to midline sites (*N1'*) when using a linked-mastoids reference.

Summary and Conclusions

- **Distinct ERP and CSD components were observed in a parallel temporal sequence for each modality, with modality-specific latencies and distinct topographies corresponding to the anatomy of visual and auditory pathways** (Fig. 4C-E; Kayser et al., 2003). **The reference-free CSD components provide a conservative, but systematic bridge between surface potentials and their underlying neuroanatomical generators.**
- **Given the longer response latencies to auditory than visual stimuli, differentially affecting old and new items** (Fig. 1), **the combined extraction of stimulus- and response-locked ERP/CSD components (i.e., their temporal and topographic characteristics) allowed a joint, direct evaluation of stimulus- and response-related *old/new effects*. Both stimulus and response onset triggered unique and common *old/new effects*.**
- **An unbiased statistical evaluation of topographical *old/new effects* was achieved through randomizations of complete component topographies** (Fig. 5; Maris, 2004).

- **A prominent *left parietal old/new effect* was observed in both modalities. Whereas stimulus-locked P3 source peaked approximately 170 ms earlier for visual than auditory tasks (longer processing time for auditory temporal analysis), but *both* sources preceded the response by about 160 ms** (Fig. 4CD).
- **Both *P3 sources* had distinct parietal topographies, with either midline (visual) or lateral (auditory) maxima, and included prominent *lateral frontocentral sinks*** (Fig. 3 and Fig. 5AB). **The overlapping old/new effects resembled auditory P3 and also included lateral frontocentral sinks, suggesting activity within a recognition memory network involving frontal and parietal regions** (e.g. Iidaka et al., 2006).
  - ➡ **Parietal and mid-frontal, *positive-going ERP old/new effects* (300-800 ms) are stimulus related (i.e., precede response onset) and originate from parietal source *and* lateral-frontal sink activity**
- **Several *post-response old/new effects* were highly comparable across modality. Lateral-frontal and inverted mid-frontal old/new effects overlapped a *mid-frontal response-related sink* (FRN) that followed and *terminated* (peak at 45 ms post-response) the *parietal and frontocentral old/new P3 source effects*.**
- **The *old/new effects* overlapping this FRN implied regional dipole activity oriented orthogonally to the cortical surface within the longitudinal fissure (anterior cingulate, supplementary motor area) with opposite orientations in the two hemispheres** (Fig. 5C) **and strongly suggest ongoing motivational or action-monitoring processes** (e.g., Donkers et al., 2005; Luu et al., 2000).
- **A further extension of this *inverted old/new effect* into off-midline centroparietal sites overlapped late SW activity across modalities** (Fig. 5C). **These observations lead to the tentative conclusion that the late episodic memory effects were triggered by the final evaluation or response decision, roughly coinciding with response onset in a paradigm that equally stressed speed and accuracy, and reflect action- or self-monitoring processes** (Johansson & Mecklinger, 2003).
  - ➡ **Late occipital, *negative-going ERP old/new effects* are triggered by the response and originate from bilateral sink activity within anterior cingulate and/or supplementary motor area**
- **The proposed methodological improvements are generic and may benefit any other ERP paradigms.**

Current Source Densities

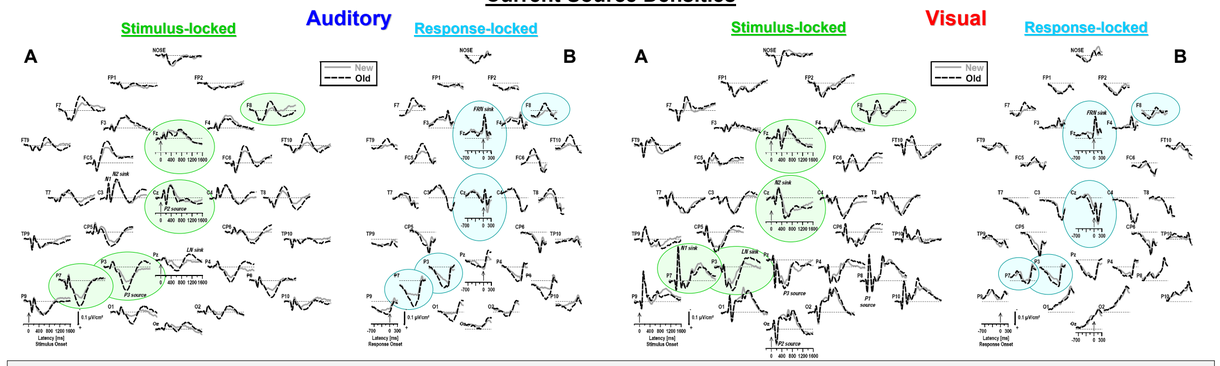


Fig. 3. Stimulus-locked (A) and response-locked (B) reference-free CSD waveforms comparing new and old auditory or visual stimuli at all 31 sites. Distinct CSD components included: Auditory stimulus-locked central N1 and N2 sinks (approximate peak latencies 120 and 420 ms at C3), central P2 (205 ms at Cz), and lateral-posterior P3 sources (635 ms at P7) and response-locked mid-frontal sinks (45 ms at Fz). Increased lateral-parietal P3 sources (P3, P7) and lateral-frontal sinks (F7, F8) were seen for old compared to new auditory stimuli. Visual stimulus-locked inferior lateral-parietal N1 sinks (approximate peak latency 150 ms at P7) and mid-parietal P3 sources (500 ms at Pz) and response-locked mid-frontal sinks (50 ms at Fz). Increased mid-parietal P3 sources (P3, Pz) and lateral-frontal sinks (F7, F8) were seen for old compared to new visual stimuli.

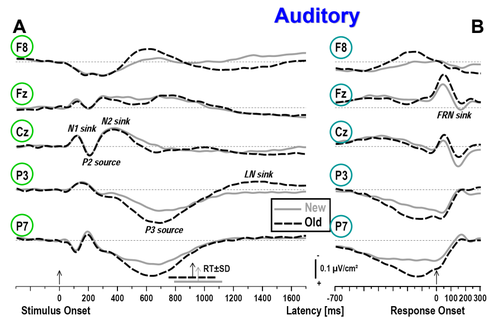


Fig. 4. Unrestricted PCA solutions using auditory or visual CSD waveforms.

A, B: Stimulus-locked (A) and response-locked (B) CSD waveforms at selected sites comparing new and old items. Mean response latencies (RT ±SD) are marked for stimulus-locked CSDs.

C, D: Time courses of Varimax-rotated covariance loadings for the first nine CSD factors extracted (85.2% and 85.6% total variance explained). Labels indicate the peak latency of the factor loadings relative to stimulus and response onsets. Factors with unique stimulus- or response-locked loading peaks are indicated by solid lines, whereas factors with both stimulus- and response-locked loading peaks are indicated by dashed lines.

E: Corresponding factor score topographies (nose at top) with percentage of explained variance. CSD factor labels consist of stimulus- and/or response-locked peak latencies of the factor loadings (brief functional interpretations are based on a signature topography). Topographies are roughly ordered by their temporal sequence, placing the unique response-locked factor (FRN sink) at the end.

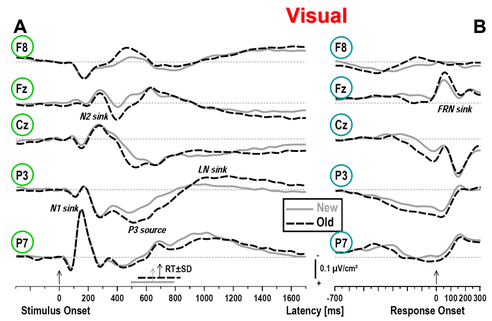
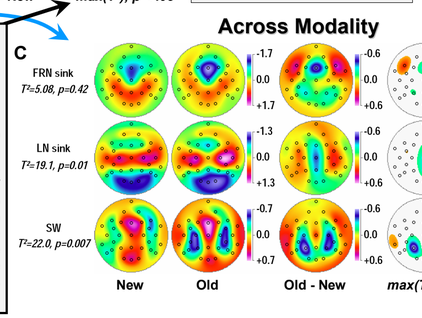


Fig. 5. Statistical evaluation of topographic old/new effects using randomization tests for three auditory (A) or visual (B) CSD factors *preceding* response onset (modality-specific P2 source, N2 sink, P3 source), and for three CSD factors *following* response onset common to both modalities (FRN sink, LN sink, SW; factor scores pooled across modality; C). Shown are the mean factor score topographies for new and old auditory stimuli, their respective difference, and significance maps.

Randomization tests (Fig. 5ABC)

Multivariate Hotelling's T^2 statistics are reported under factor labels to the left.

Squared univariate (channel-specific) paired samples *T* statistics thresholded at the 95th quantile (*p*=.05) of the corresponding randomization distribution (maximum of all 31-channel squared univariate paired samples *T* statistics) are plotted as maps to the right. To facilitate comparisons of the max(T^2) topographies with the underlying sink-source difference topographies, the sign of the difference at each site was applied to the respective T^2 value, which is otherwise always positive.



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