Abstract

orted that depressed patients (N=25) had reduced novelty P3 compared to healthy controls 31-channel montage. We report here an independent replication and extension (49 patients;) using 67 channels. A novelty oddball task (Friedman et al., 1993) included two 300-ms s: 350 Hz, p=.76; targets: 500 Hz, p=.12) and novel sounds (e.g., dog bark, human cough: 12) in pseudorandom order at 1000 ms ISI using eight 50-trial blocks. Participants ickly as possible to target tones only, with response hand counterbalanced across blocks. urrent source densities (CSDs; spherical spline Laplacian) derived from ERP waveforms and measured using temporal, covariance-based principal components analysis (PCA), estricted Varimax rotation. Extracted factors were consistent with those reported for a (Kayser & Tenke, 2006a,b) including: N1 (120 ms loadings peak), P2/N2 (245 ms), early l late P3 (568 ms). Factor 351 efficiently summarized P3b sources (medial parietal rgets), but included a secondary midline frontocentral source for novel and target stimuli. 5, a midcentral source (Cz maximum) was present for novels but absent for targets, and reduced in patients. Spatiotemporal PCA confirmed the specificity of this early midcentral s. Results are consistent with a reduced novelty response in clinical depression, involving P3 and P3b generators.

Introduction

reports of reduced P3 amplitude in depressed patients may, in part, be due to the multiple comprising the late positive complex, each arising from distinct neural generators and different cognitive processes. We recently reported that depressed patients (N=25) had P3 compared to healthy controls (N=23) using a 31-channel montage (Kroppmann, et al., t here an independent replication and extension (49 patients; 49 controls) using 67 channels ensity montage and reference-free methodology.

Methods

depressed outpatients (22 male; age = 35.8 ±10.7 yrs) and 49 healthy adults (23 male; age = vith no history of any psychopathology or neurological disorder. Participants were ght-handed (Edinburgh Handedness Inventory LQ: Controls = 83.2 ± 21.9; Patients = 63.2 onfirmed after excluding left-handed participants).

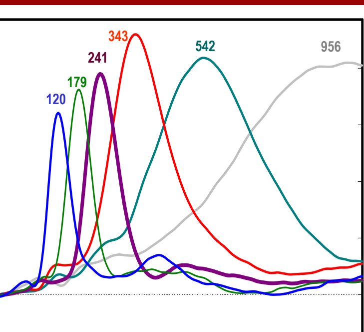
n and Artifact Procedures: Continuous EEG was recorded using a 72-channel Biosemi em (256 sps) . Data were rereferenced to nose, bipolar EOG derivations computed, and roscan format using Polyrex (Kayser, 2003) and blink corrected (spatial PCA routine; nulus-locked epochs (1200 ms, 200 ms prestimulus) were extracted. EEG channels fier drift, residual eye activity, muscle or movement-related artifacts or noise for any given fied using a reference-free approach (Kayser & Tenke, 2006c), and replaced by spherical ons (Perrin et al 1989) using the data from artifact-free channels if possible (i.e., less than nels contain an artifact), as verified by visual inspection. ERP averages were computed for ontargets and novels (n>15 for all averages), as well as for Novels in the first and last ols, 44 patients, n>8).

l Hemispatial PCA: Reference-independent CSD waveforms were computed from ERPs l spline surface Laplacian (Perrin et al, 1989; 50 iterations; m = 4; λ = 10-5). CSDs were poral PCA (covariance matrix, unrestricted Varimax rotation; Kayser & Tenke, 2003, pproach yields distinctive PCA components (factor loadings waveforms) and corresponding cients (factor score topographies), which concisely simplify and quantify the temporal al distribution of underlying neuronal generators. These results were compared to those tial PCA (spatial PCA based on hemitopographies, Tenke et al, in press) to assure that the are not due to misallocated temporal variance.

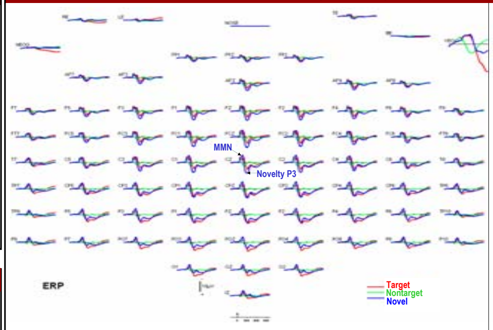
ods: CSD topographies allow simplified analyses of well-defined regions. Based on *a priori* nds and the observed topography of the Novelty P3 source, a repeated measures ANOVA four midline sites (Fz, FCz, Cz, CPz; cf Figs. 1-2). Only Novelty effects reported here.

task: An auditory novelty oddball task (Friedman et al., 1993) was implemented on a M system. For each subject, 8 blocks of 50 trials consisting of two 300 ms tones are udorandom order (stimulus onset asynchrony = 1000 ms). One nontarget tone of 350 Hz is subject frequently (p = .76) while the other is an infrequent 500 Hz target tone (p = .12). e., animal sounds, musical instruments, environmental sounds) possessing durations of 100- quently (p = .12) intermixed with the frequent tones and infrequent target tones. All stimuli naurally over headphones at 75 db SPL. Subjects are instructed to focus their eyes on a splayed on a computer monitor and to respond with a button press as quickly as possible when, they hear the infrequent target tones. Response hand (right or left) was across blocks.

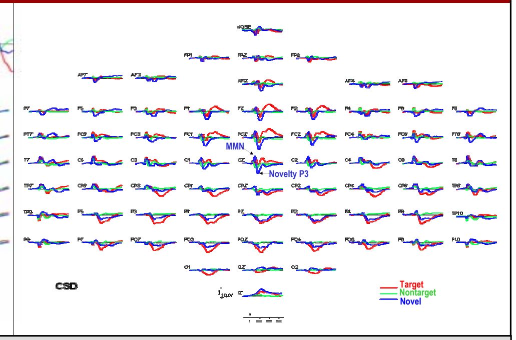
IIIA. Temporal PCA Solution: Loadings



I. Nose-referenced surface potentials (ERPs)

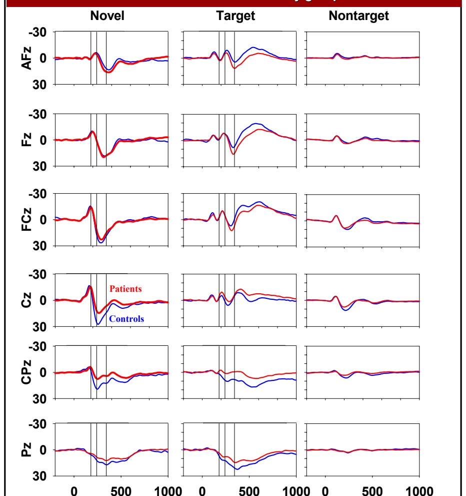


Surface Laplacians (CSDs)



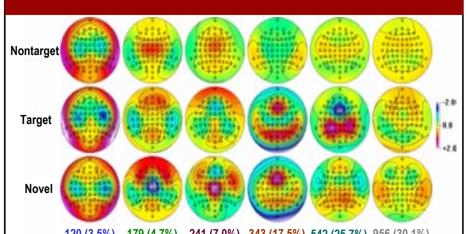
Grand average ERP (left) and CSD (right) waveform topographies for correct targets, nontargets, and novels

II. Midline CSD waveforms by group



Averaged midline CSD waveforms for patients and healthy controls for Novels (left column), Targets (center) and Nontargets (right). For Novels, a short latency sink (MMN) is followed by a source (Novelty P3) at central sites (CPz, Cz) and but is attenuated and delayed at anterior sites (peak latency approximates Target-P3).Vertical lines indicate peak latencies of CSD-PCA factors of interest

IIIB. Temporal PCA Solution: Factor Score Topographies



Factor Score Topographies of first six factors. Correct Nontargets, Targets and Novels

Table 1 **Comparison of Varimax-rotated CSD-PCA initial components for Novelty with Dichotic and Binaural oddball tasks**

Novelty Oddball		Dichotic Oddball [1]		Binaural Oddball [2]		Interpretation [3]
Peak Latency [ms]	Explained Variance	Peak Latency [ms]	Explained Variance	Peak Latency [ms]	Explained Variance	
120	3.49	105	4.8%	105	4.5%	N1−
179	4.66	150	2.3%	160	3.9%	Temporal lobe N1−; MMN− for Novel
241	6.95	245	3.6%	215	5.3%	N2−; P3+ for Novels
343	17.49	440	30.3%	355	23.0%	P3+; P3+ for Novels

Summary of Results

Comparable CSD-PCA factor structure for Novelty, Conventional and Dichotic oddballs tasks

- N1 (120 ms peak) sink/source topography is comparable for Targets, Nontargets and Novels, and consistent with activation of primary auditory cortex within the Sylvian fissure
- A subsequent sink (temporal N1; 179 ms) consistent with generators on the lateral surface of the temporal lobes, was observed for Targets, Nontargets and Novels
- Target-related P3 source (343 ms) is over parietal regions
- Target-related N2/P3 sequence (241 sink/ 343 source) evident

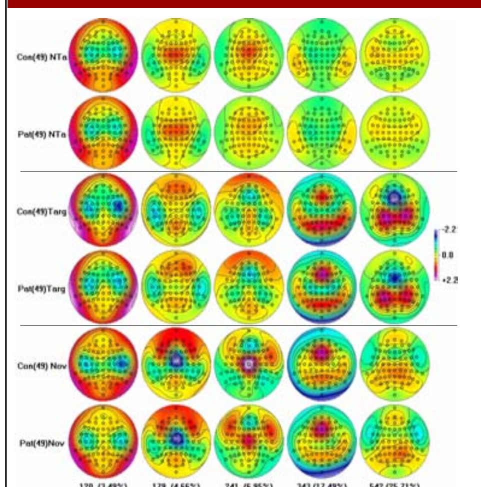
Unique to Novelty oddball task

- Frontal Target-N2 (241 ms) sink has a midline topography
- Target-P3 (343) source has secondary topography on frontal midline

Unique to Novel stimuli

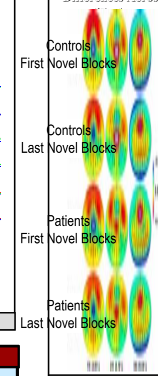
- Central midline sink concurrent with temporal N1 (MMN sink; 179 ms)
- Central midline source at N2-latency (Novelty P3 source; 241 ms)

IV. Factor Score Topographies by Group



Group differences in CSD-PCA factor score topographies. Patients show a marked reduction in early source activity (241 ms) at Cz to Novels (lower rows). This difference is not evident for the later P3 source (343), or for the preceding MMN sink (179).

V. Reproducibility of Solution and Group Differences Across

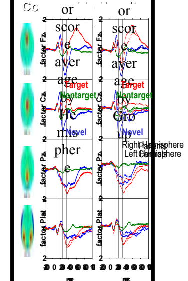


PCA based on 4 conditions (Novels-1st half, Novels-2nd half, Nontargets, Targets) yielded comparable factors with similar differences in factor score topographies between groups.

Conclusions

- Novelty P3 source is reduced in Depressed Patients, but the reduction is **restricted** to the **earliest onset** of the P3 source (241 ms) at **central** sites

VI. Hemispatial PCA



Hemispatial factor loadings (maps) and factor score waveforms for Targets, Nontargets and Novels. *Left*. Factor score waveforms for the two hemispheres (identical colors) are closely comparable. Reference lines indicate peak latencies of the three factors of interest from the temporal CSD-PCA. *Right*. Averages across hemispheres for healthy controls (solid lines) and patients (dashed lines) for Targets, Nontargets and Novels support the identification of Group differences at Cz as the novelty P3 source and distinct from a later target-related P3 source.

References

Friedman, D., Simpson, G., & Hamberger, M. (1993). Age-related changes in scalp topography to novel and target stimuli. *Psychophysiology*, 30(4), 383-396.

Kayser, J. (2003). Polygraphic Recording Data Exchange - PolyRex (*http://psychophysiology.cpmc.columbia.edu/PolyRex.htm*). New York State Psychiatric Institute: Department of Biopsychology.

Kayser, J., Tenke, C. E. (2003). Optimizing PCA