Novelty P3 Reductions In Depression: Characterization Using CSD-PCA

Cognitive Neuroscience, New York State Psychiatric Institute and University College of Physicians & Surgeons, New York

Abstract

We recently reported that depressed patients (N=21) had reduced novelty P3 compared to healthy controls (N=25) using a 2-channel montage (Cz-Pz) or using 6-channel montages (Cz-Pz-C3-P4-Fz-F3). A novelty oddball task (Friedman et al., 1993) included two 300 ms tones (nontargets: 350 Hz, p=.76; targets: 500 Hz, p=.12) and novel sounds (e.g., dog bark, human cough 100-400 ms, p<.02) in pseudorandom order at 1.000-1.250 ms after stimulus onset. Participants responded as quickly as possible to target tones only, with response hand counterbalanced across blocks. Reference-free current source densities (CSDs), spherical spline Laplacian derived from ERP waveforms were simplified and measured using temporal, covariance-based principal components analysis (PCA), followed by annotated Varimax rotation. Extracted factors were consistent with those reported for a standard oddball (Kaye & Tenke, 2006a,b) including: 1) (120 ms leads peaks, P252 (241 ms), early P3 (151 ms), and late P3 (236 ms). Factor 2) (343) consisted of anterior P200 sources (medial parasit maximum for target), but included a secondary midline frontocentral source for novel and target stimuli. Within factor 2, a midcentral source (max) was present for novels but absent for targets, and was significantly reduced in patients. Spatiotemporal PCA confirmed the specificity of this early midcentral source for novels. Results are consistent with a reduced novelty response in clinical depression, involving multiple novelty P3 and P3b generators.

Introduction

The conflicting reports of reduced P3 amplitude in depressed patients may, in part, be due to the multiple subcomponents comprising the data positive complex, such as existing from distinct neural generators and associated with different cognitive processes. We recently reported that depressed patients (N=21) had reduced novelty P3 compared to healthy controls (N=25) using a 10-channel montage (Kroppmann, et al., 2008). We report here an independence replication and extension (49 patients; 49 controls) using 67 channels utilizing a higher density montage and reference-free methodologies.

Methods

Participants: 49 depressed outpatients (22 male; age = 35.8 ± 10.7 yrs) and 49 healthy controls (23 male; age = 35.0 ± 10.7 yrs) with no history of any psychopathology or neurological disorder. Participants were predominantly right-handed (Edinburgh Handedness Inventory: L-R = 85.2 ± 23.9; Pattern = 6.2 ± 4.7); results confirmed after excluding artifacts (10 participants).

EEG: Acquisition and Artifact Procedures: Continuous EEG was recorded using a 72-channel BrainAmp ActiveTwo system (256 Hz). Data were referenced to nose.剥离 EEG derivatives computed, and exported to Neuroscan format using Polysign (Kaye, 2005) and Hink corrected (spatial PCA routine; Neuroscan). Stimulus-locked epochs (200 ms, 200 ms poststimulus) were extracted. EEG channels containing amplification drift, residual eye activity, muscle or movement-related artifacts or noise for any given trial were identified using an interactive approach (Kaye & Tenke, 2006a) and replaced by spherical spline interpolations (Perrin et al, 1989) using the data from artifact-free channels if possible (i.e., less than 25% of all channels contain an artifact), as verified by visual inspection. ERP waveforms were computed for correct targets, nontargets and novels (15 ± 5 for all analyses, as well as for Novel in the first and last halves 46 controls, 46 patients, ± 8).

CSD – PCA and Reference-independent CSD waveforms were computed from ERPs using a spherical spline Laplacian (Perrin et al., 1989). MMN (max; m = 4; λ = 10-5) and Novelty P3 (max; m = 4; λ = 10-5) were extracted from ERP waveforms for novel or target stimuli. ERP waveforms were simplified using spatial covariance-based principal components analysis (PCA), followed by annotated Varimax rotation. Extracted factors were consistent with those reported for a standard oddball (Kaye & Tenke, 2006a,b). Within factor 2, a midcentral source (max) was present for novels but absent for targets, and was significantly reduced in patients. Spatiotemporal PCA confirmed the specificity of this early midcentral source for novels. Results are consistent with a reduced novelty response in clinical depression, involving multiple novelty P3 and P3b generators.

Novelty oddball task: An auditory novelty oddball task (Friedman et al., 1993) was implemented on a Nicolet Neuroscan system. For each condition two blocks consisting of two 500 ms tones are presented in pseudorandom order (stimulus onset-asynchrony = 1000 ms). One nontarget tone 350 Hz is presented to the subject frequently (p = .76) while the other is an infrequent 500 Hz target tone (p = .12). Novel sounds (i.e., animal sounds, musical instruments, environmental sounds) possessing durations of 100-400 ms are infrequently (p = .12) presented with the frequent tone and infrequent target tones. All stimuli are presented binaurally over headphones at 75 dB. Subjects are instructed to focus their eyes on a fixation point presented counterbalanced across blocks.

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Conclusion

Patients, but the selection is restricted to the earliest onset of the P3 component.