

Abstract

Recent interest in loudness dependency of auditory evoked potentials (LDAEP) owes largely to its promise as a predictor of clinical response to treatment with serotonin agonists. Originally based on peak-to-peak N1/P2 differences, LDAEP has been quantified by inverse models as N1 activity attributable to primary auditory cortex (e.g., BESA tangential dipole; LORETA current density). However, reference-free, scalp-recorded current source density (CSD; surface Laplacian) and temporal PCA together allow simplification and separation of overlapping component waveforms and topographies that are obscured in ERPs by volume-conduction and superposition. Because CSD-PCA provides a conservative, model-independent approach to the problem of generator localization, we used unrestricted, Varimax-rotated temporal CSD factors (covariance matrix) to quantify scalp current source and sink patterns underlying LDAEP. Auditory ERPs were recorded from a 72-channel BioSemi ActiveTwo system in 16 healthy adults while they listened to pure (1000 Hz), 40-ms binaural tones (1600-2100 ms ISI) presented at five, equiprobable intensities (60-100 dB SPL). An N1 factor (loadings peak: 116 ms) with the expected tangentially-oriented sink/source topography consistent with activation of auditory cortex showed a robust, monotonic association with intensity. Likewise, a P2 factor (222 ms) with a midline source topography also showed intensity effects; however, these were less robust and included variable secondary sources at frontotemporal sites. In contrast, no significant association with loudness was observed for a radial temporal lobe N1 sink (167 ms) or for a temporal lobe P3 source (343 ms). Moreover, loudness dependency of N1 was not statistically improved for combined topographies (e.g., sums/differences of N1 with P2/temporal N1). Thus, CSD-PCA offers a concise and efficient, but conservative, characterization of LDAEP generators.

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Methods

Participants. 23 healthy adults (12 male; age = 32.3±9.2 yrs) with no history of any psychopathology or neurological disorder, all subjects right-handed (Edinburgh Handedness Inventory LQ=79.6 ± 20.0).

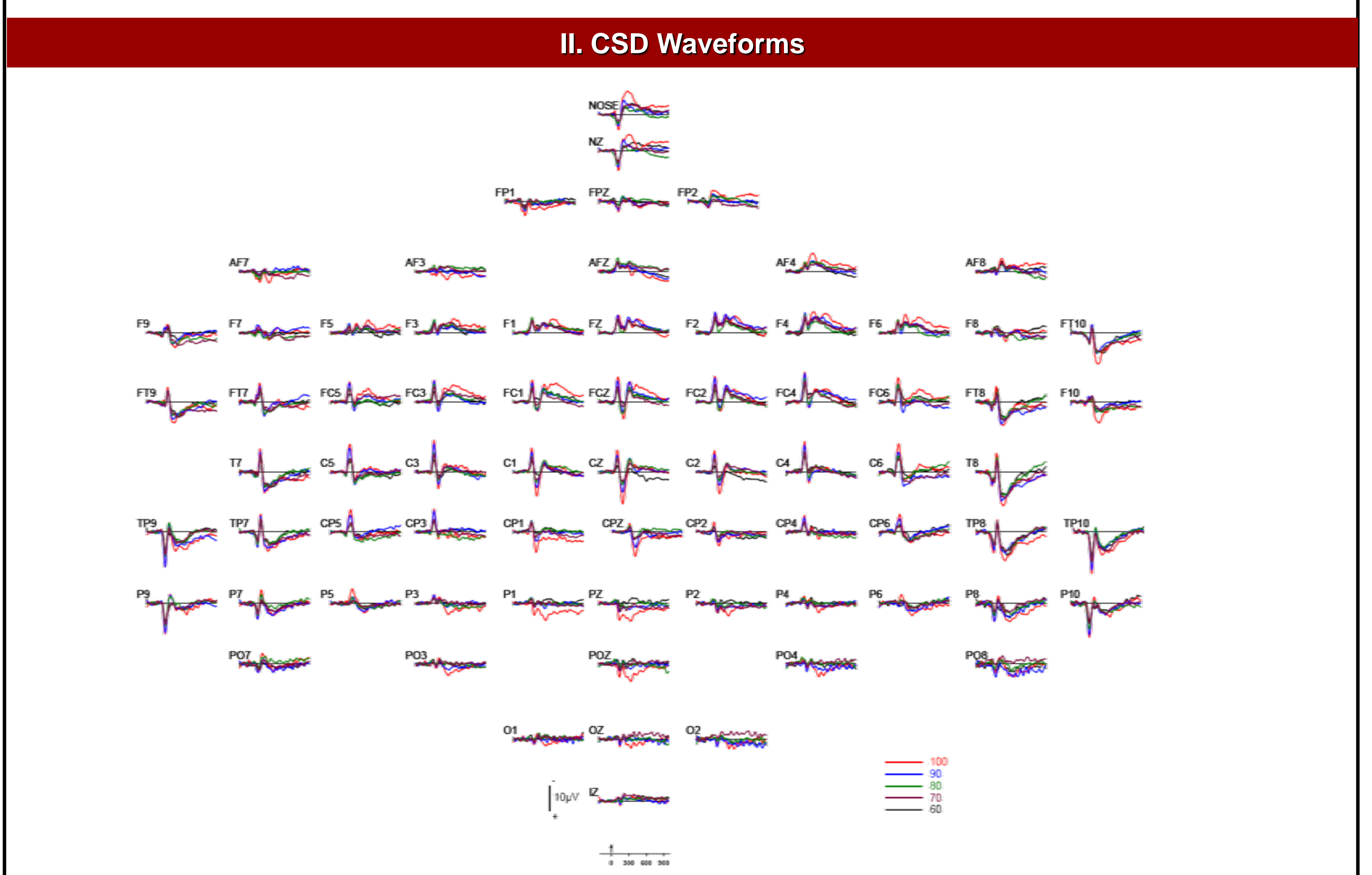
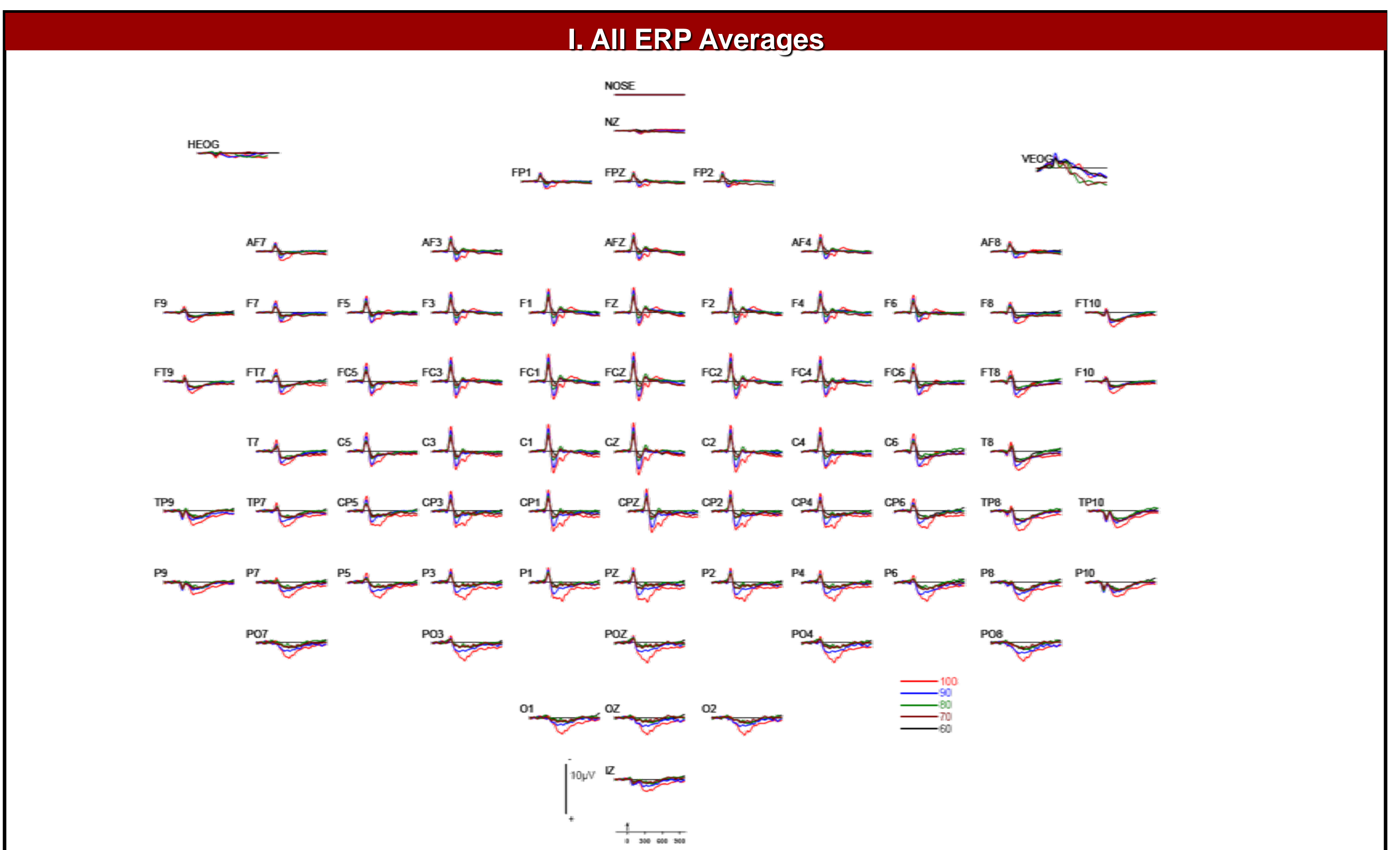
Intensity modulation. Subjects sit quietly with their eyes opened and fixed on a cross while binaural tones (1000 Hz, 40 ms duration with 10 ms rise and decay time) are presented at varying levels of intensity (e.g., Hegerl & Juckel 1993; Juckel et al 2003). Tones are presented in pseudorandomized order via TDH-49 headphones at five intensities (60, 70, 80, 90, 100 dB SPL) with interstimulus intervals ranging from 1600 – 2100 ms. Each stimulus intensity is repeated 100 times (i.e., 5 stimulus intensities = 500 trials).

ERP recordings. ERPs were recorded from 72 scalp sites (ActiView; BioSemi), using an active recording reference composed of sites PO1 (common mode sense) and PO2 (driven right leg), and referenced to nose offline. Continuous data were exported to Neuroscan format using Polyrex (Kayser, 2003). Amplifier drift was eliminated by padding the beginning of the file and applying a rectangular high-pass filter (10 s time constant). Continuous EEG blink corrected using a spatial, singular value decomposition (NeuroScan). Stimulus-locked epochs (1200 ms, 200 ms prestimulus) were extracted and screened for electrolyte bridges (Tenke & Kayser, 2001). Channels containing amplifier drift, residual eye activity, muscle or movement-related artifacts or noise for any given trial were identified using a reference-free approach (Kayser & Tenke, 2006c), and replaced by spherical spline interpolations (Perrin et al., 1989) when possible. ERP averages were then low-pass filtered at 12.5 Hz (-24 dB/octave) and finally baseline-corrected using the 200 ms preceding stimulus onset.

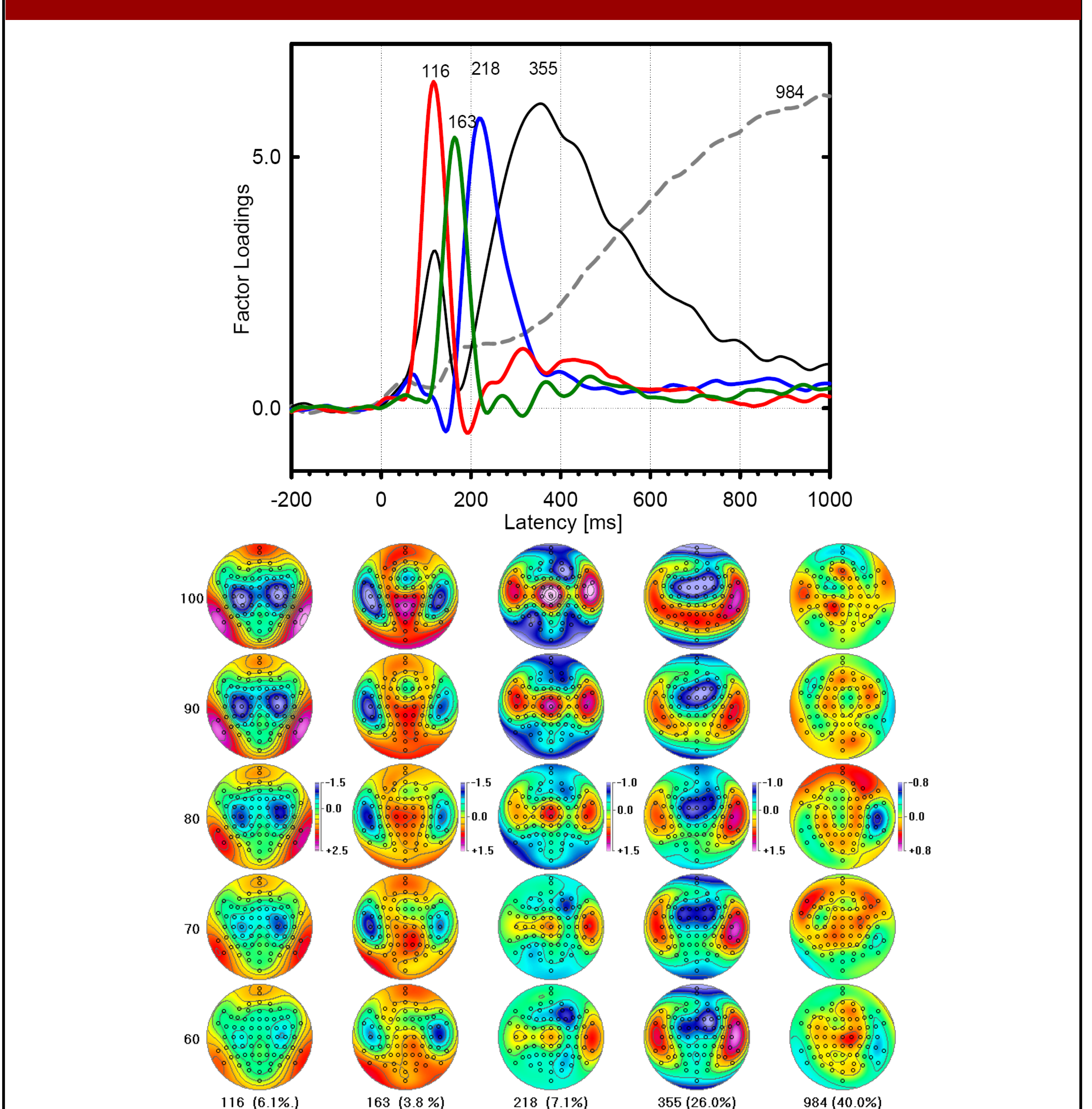
ERPs were averaged for each stimulus intensity. For the purpose of intensity modulation, the tangentially-oriented N1 generator within the superior temporal gyrus in the vicinity of primary auditory cortex is uniquely important (Hegerl & Juckel 1993; Mulert et al 2002). Although CSD-PCA dissociates this tangential N1 generator from a radially oriented, temporal lobe subcomponent of N1 (temporal N1 factor; cf. Kayser & Tenke 2006a,b), we examined all components of interest in the course of our analytic approach. In deference to the literature of the task, which focuses on N1-P2 differences (e.g., Gallinat et al 2000), we also explored N1-minus-P2 difference topographies.

CSD. Reference-free CSD waveforms (spherical spline Laplacian; Perrin et al., 1989) were computed from ERP averages to sharpen topographies, eliminate volume-conducted contributions from distant regions, and quantify underlying current generators (Kayser & Tenke, 2006; Tenke & Kayser, 2005).

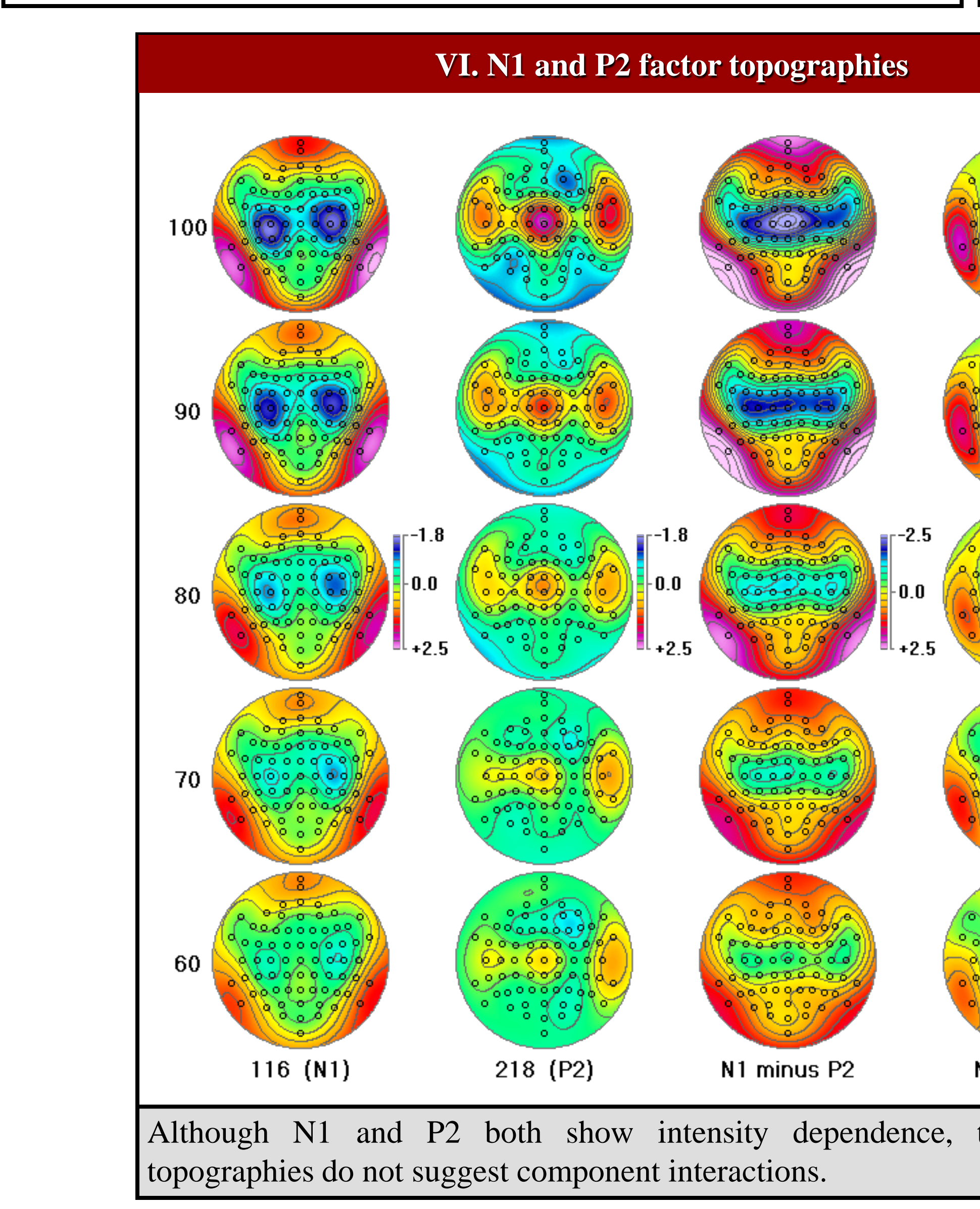
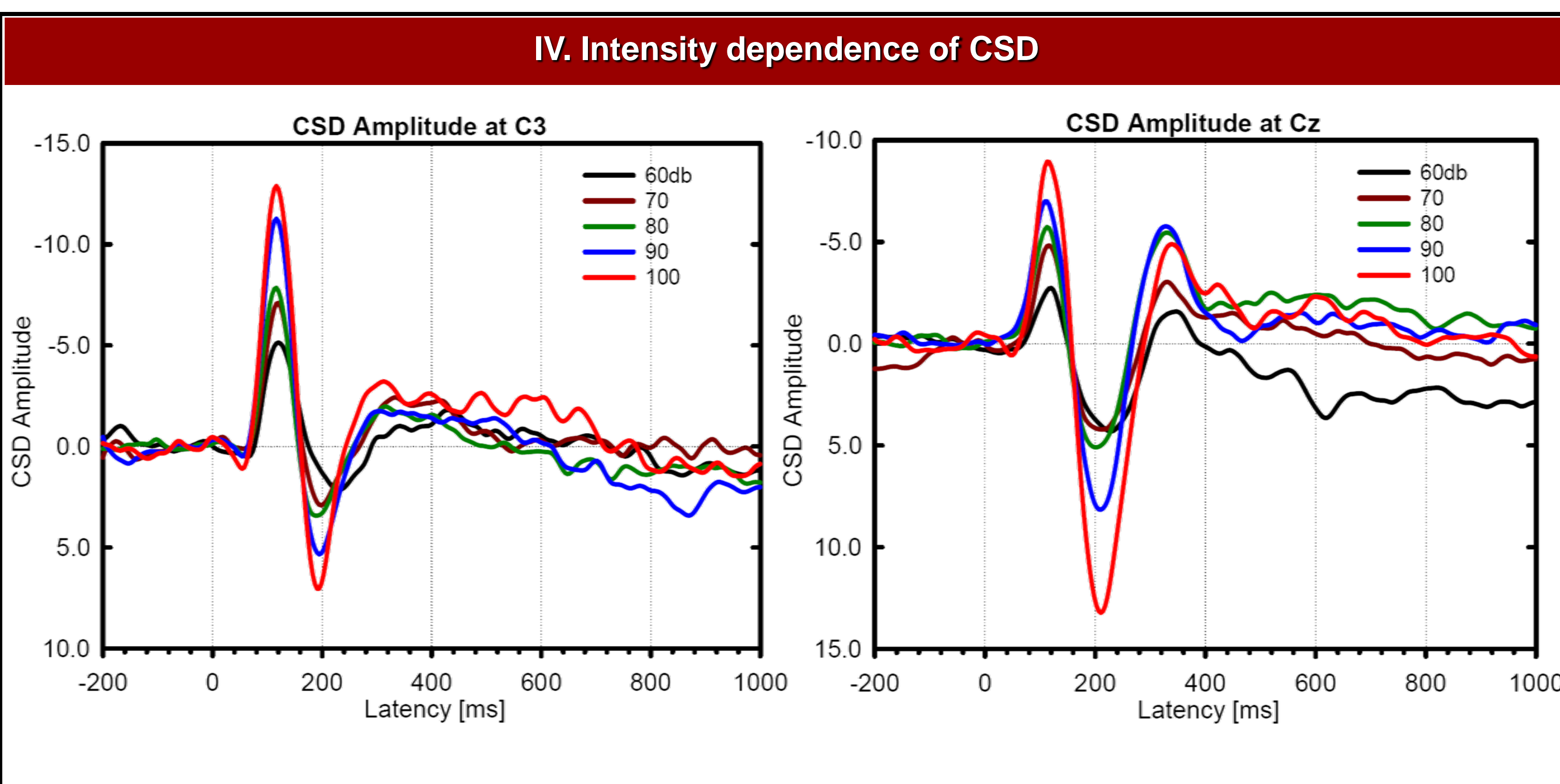
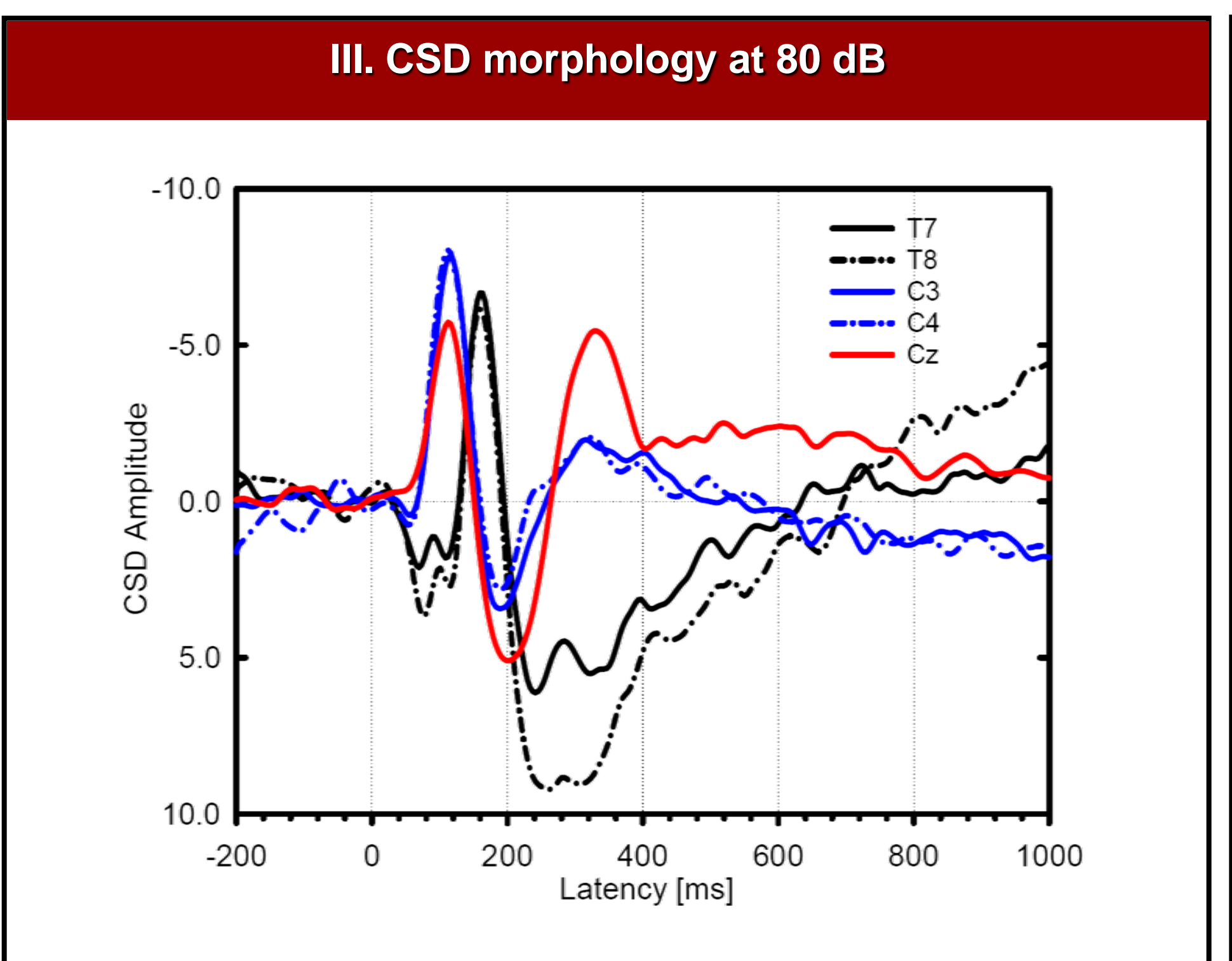
CSD-PCA. CSDs were submitted to unrestricted PCA using the covariance matrix (308 variables = samples -200 to 1000 ms; 8280 observations = [23 Subjects x 5 Conditions x 72 Sites]) followed by Varimax rotation (Kayser & Tenke, 2003). For each PCA factor of interest, factor scores were submitted to repeated measures ANOVA using within-subjects factors electrode Site and Condition (100, 90, 80, 70, 60 dB) for midline regions (e.g., vertex), and Hemisphere (right/left) for sites off the midline.



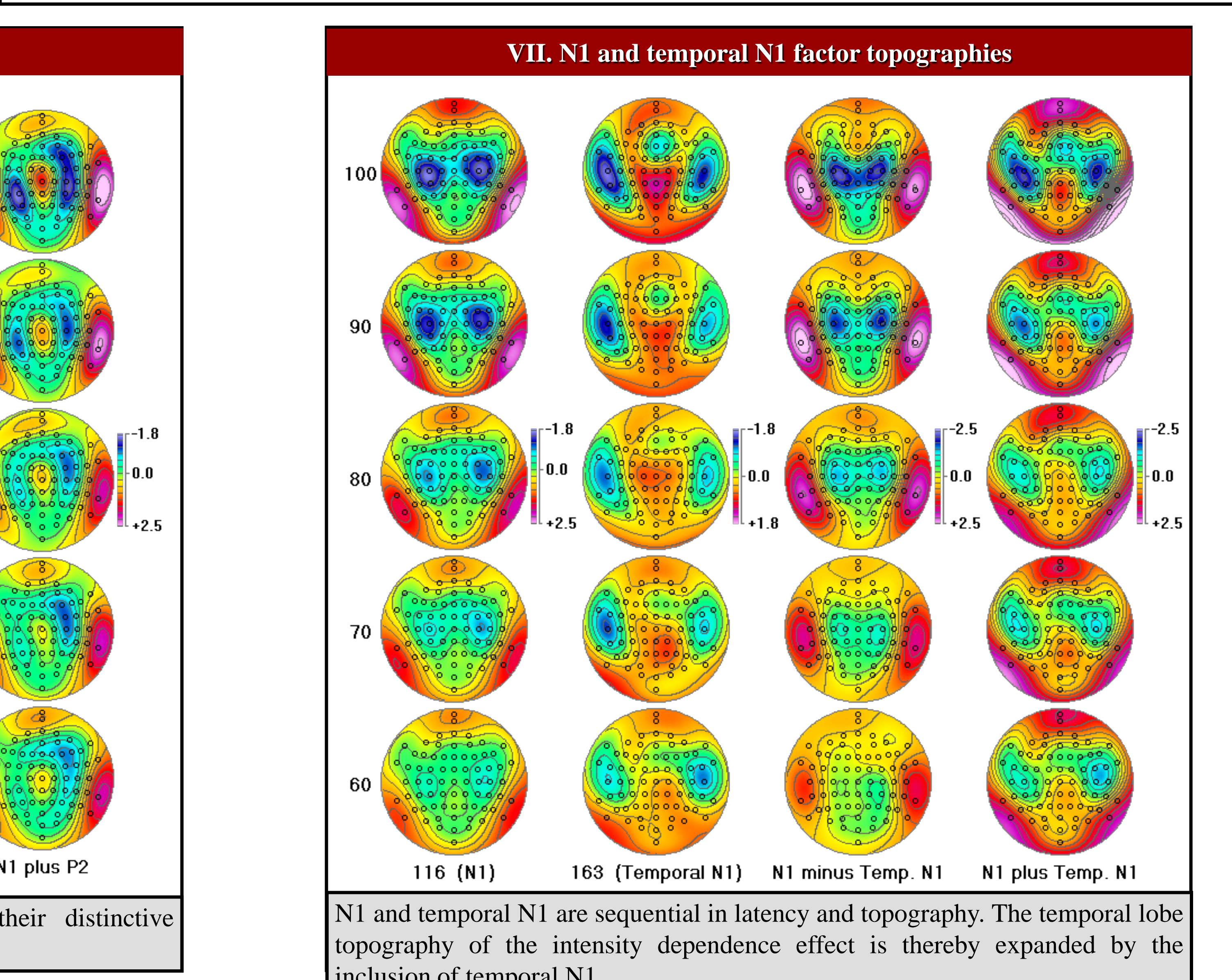
V. Varimax Rotated Factor Loadings and Factor Score Topographies



PCA Factor loadings waveforms and factor score topographies for 5 factors with largest variance contributions, and corresponding averaged factor score topographies for each stimulus intensity (arranged by peak latency). Maps scaled per factor to optimize intensity effects

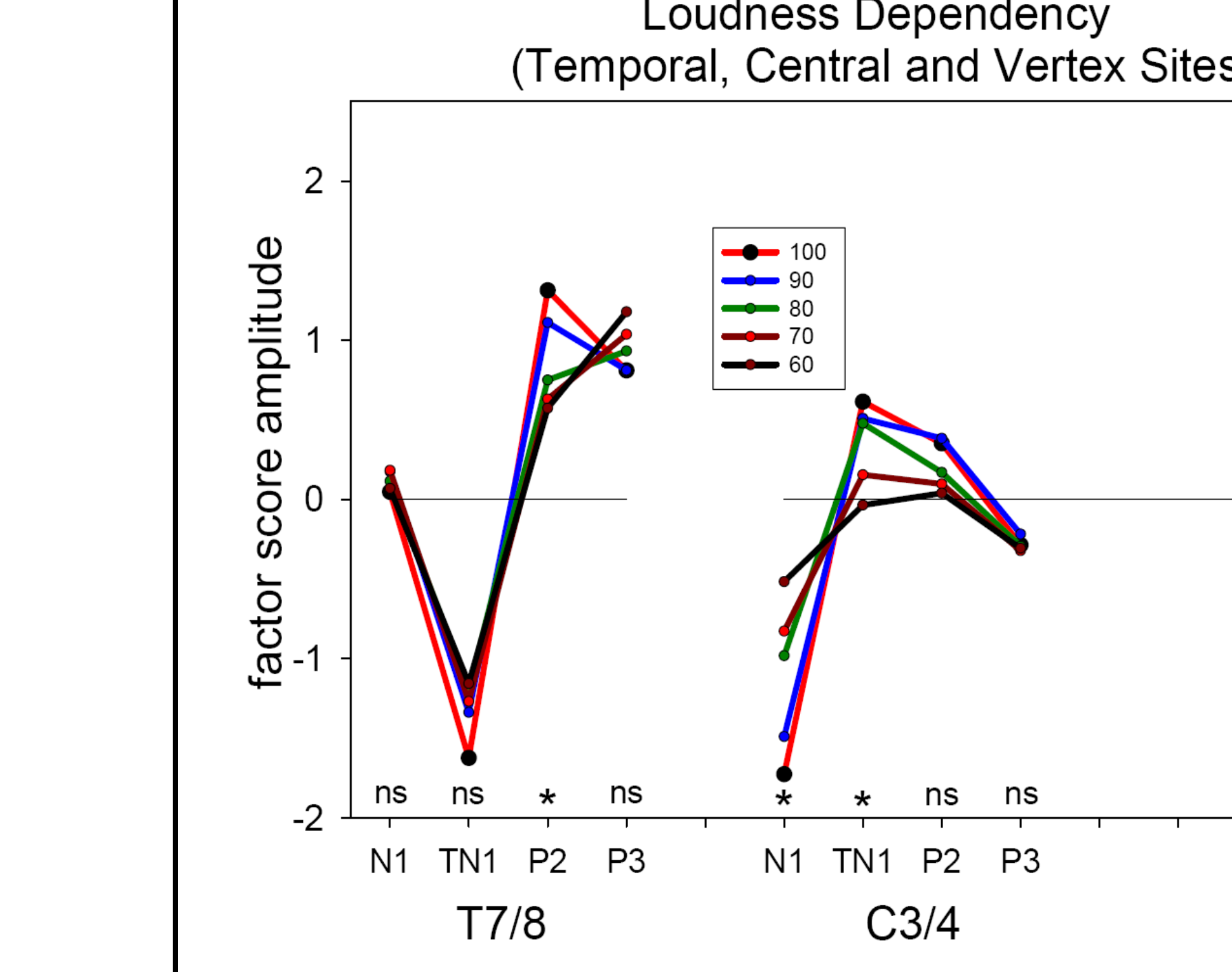


Although N1 and P2 both show intensity dependence, their distinctive topographies do not suggest component interactions.



N1 and temporal N1 are sequential in latency and topography. The temporal lobe topography of the intensity dependence effect is thereby expanded by the inclusion of temporal N1.

VIII. N1 and P2 factor topographies



An N1 factor (loadings peak: 116 ms) with the expected tangentially oriented sink/source topography consistent with activation of auditory cortex showed a robust, monotonic association with intensity. Likewise, a P2 factor (218 ms) with a vertex source topography also showed intensity effects. The P2 topography also included secondary sources at frontotemporal sites that were variably related to intensity, attaining statistical significance at T7/8.

In contrast to the separable latencies and topographies of N1 and P2, the radial temporal lobe sink (temporal N1), reflects the continuation of the processing characterized by N1. Consequently, the intensity dependence of temporal N1 was not statistically reliable where the sink was maximal (T7/8), its corresponding source showed a significant intensity effect at C3/4 (i.e., where the N1 sink is maximal).

A subsequent temporal lobe P3 source (355 ms) did not show a consistent intensity-dependent topography.

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Conclusions

- CSD-PCA offers a concise and efficient, but conservative, characterization of temporal lobe generators underlying the loudness dependency of N1.
- The loudness dependency of P2 does not arise from temporal lobe processes