

LOUDNESS DEPENDENCY OF MISMATCH NEGATIVITY (MMN): EVIDENCE FROM CSD-PCA

Nathan A. Gates¹, Craig E. Tenke^{1,2}, Daniel M. Alschuler¹, Christopher J. Kroppmann¹, Gerard E. Bruder^{1,2}, Jürgen Kayser^{1,2}

¹ Division of Cognitive Neuroscience, New York State Psychiatric Institute, New York, NY;

² Department of Psychiatry, College of Physicians and Surgeons, Columbia University, New York, NY

NEW YORK STATE
Psychiatric Institute

COLUMBIA PSYCHIATRY

Poster available in high resolution at
<http://psychophysiology.cpmc.columbia.edu/mmedia/spr2009/MMN.pdf>

Overview

Background: The loudness dependency of the auditory evoked potential (LDAEP) is shown in a passive task in which each of a range of intensities is presented with equal, but low, probability, yielding a reliable relationship between N1/P2 and loudness. However, the impact of overlapping MMN and other salience-driven ERP components (e.g., P3a, Novelty P3) generated by large intensity disparities between consecutive tones in this paradigm has not been studied. Conversely, it is unclear to what extent the MMN produced by loud and soft tones is affected by stimulus intensity.

Methods: Binaural tones (1000 Hz; 40-ms; 500 ms ISI) were presented at four intensities (70, 80, 90, 100 dB SPL) in a modified MMN task, in which one of the four intensities was used as a frequent standard (70%), and the remaining three as infrequent deviants (10% each), in each of four blocks, counterbalanced across subjects (Fig. 1). Intensity-dependency of N1/P2 was validated against a standard LDAEP paradigm (see Poster 64) for a stimulus block of equiprobable intensities (70-100dB SPL) with the same short, fixed ISI (Fig. 2). Healthy adults (N = 33) watched a silent film to direct the subject's attention away from the auditory stimuli, and reported its content (underwater scenes) after each block. Using 72-channel ERPs, temporal principal components derived from reference-free current source density (CSD) waveforms characterized neuronal generator patterns underlying intensity-dependency of N1-P2. A second principal components analysis (PCA) was performed for difference CSD waveforms (deviant-minus-standard) calculated from comparable deviant and standard conditions at each intensity level (e.g., 100dB deviant-minus-100dB standard) to isolate activity related to deviance (i.e., MMN).

Results: Factors related to N1-P2 (Fig. 4) included: 1) N1 sink (113 ms peak; tangential sink/source topography); 2) temporal N1 sink (159 ms; radial temporal lobe sink); 3) P2 source (214; midline and bilateral temporal sources). These three factors revealed monotonic increases with intensity for standard and deviant stimuli. PCA factors derived from the CSD difference waveforms (Fig. 6) included: 1) relative MMN sink (136 ms peak; tangential sink/source topography); 2) relative vertex source (230 ms peak). The MMN sink was characterized by a late, N1-like tangential sink/source topography that increased with the level of stimulus disparity (+/- dB) and was most pronounced for louder tones. The vertex source was observed solely in the loudest deviants, likely reflecting P3a to these salient tones.

Conclusions: N1/P2 LDAEP and MMN/P3a to stimulus disparity/salience may both be measured in the same task.

Stimuli and Procedure

Basic Design

Block	70% Probability ("Standard")	10% Probability ("Deviant")	10% Probability ("Deviant")	10% Probability ("Deviant")
A	70 dB	80 dB	90 dB	100 dB
B	80 dB	70 dB	90 dB	100 dB
C	90 dB	70 dB	80 dB	100 dB
D	100 dB	70 dB	80 dB	90 dB
Block	20% Probability ("Equiprobable")	20% Probability ("Equiprobable")	20% Probability ("Equiprobable")	20% Probability ("Equiprobable")
E	70 dB	80 dB	90 dB	100 dB

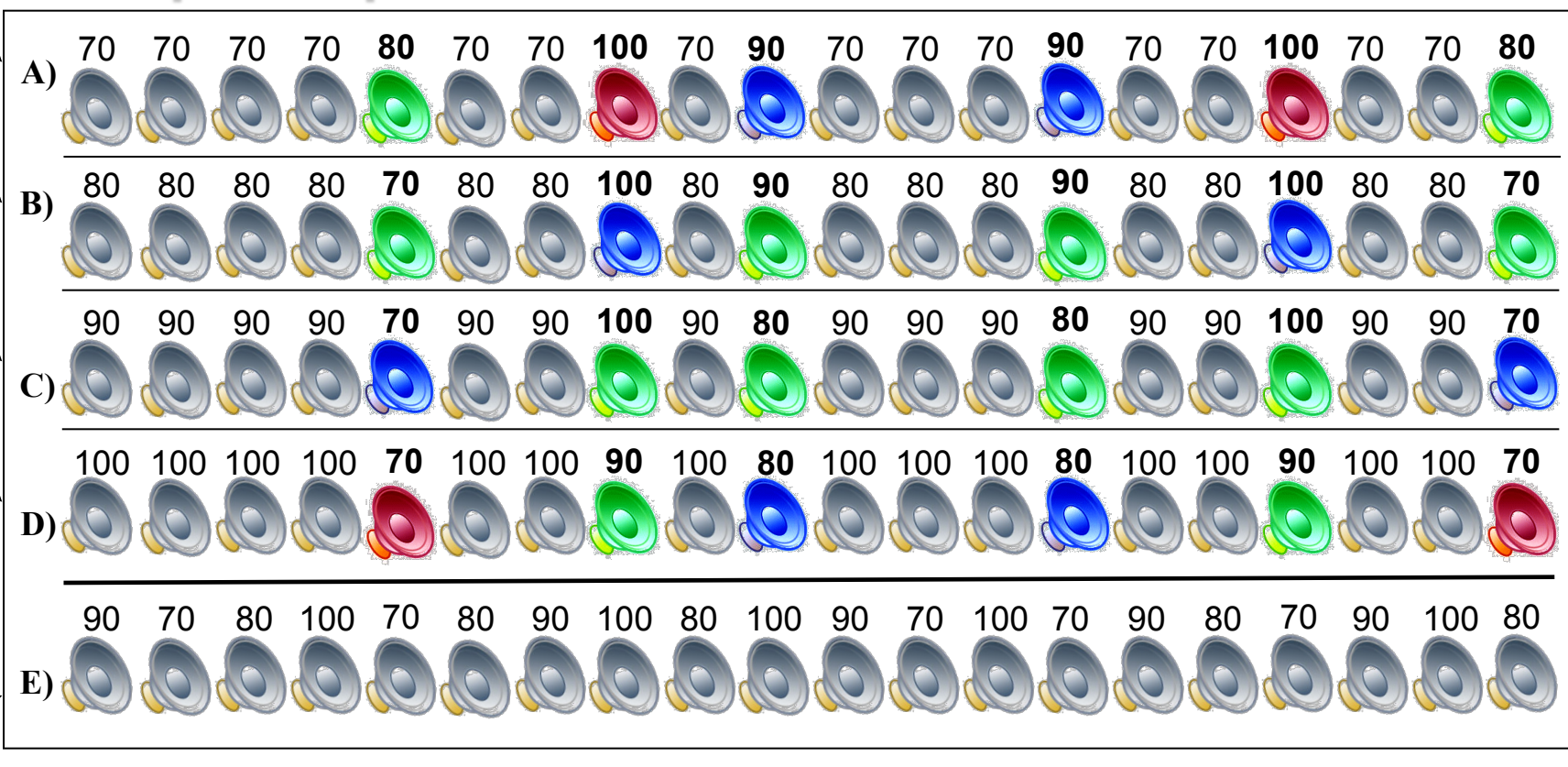
Figure 1. Study Design: Tones were presented at four levels of intensity (70, 80, 90, 100 dB) and occurred at two levels of probability in four experimental blocks. For each block, one intensity was presented as a standard (70%) and the three remaining intensities as deviants (each at 10% probability; see A–D). An additional block (block E) of equiprobable intensities served as a standard intensity-modulation paradigm to validate intensity effects on N1-P2.

Magnitude of Deviance

70 dB +/- 10 dB 80 dB +/- 20 dB 90 dB +/- 30 dB

1000 Hz Sine Tones
40 ms (10 ms rise/fall) Duration
500 ms SOA

Example Sequences



Example segments of each experimental block. The magnitude of intensity discrepancy between each deviant and standard tone are shown as:

+/- 10 dB
+/- 20 dB
+/- 30 dB

400 stimuli consisting of 280 standards and 120 deviants (40 per deviant intensity) were counterbalanced and pseudorandomized across blocks A–D. Block order was counterbalanced across subjects.

- Presentation® stimulus delivery and experimental control software (Neurobehavioral Systems Inc., 2008) was used to calibrate and deliver the experimental tones through the computer sound card. A 20-s 1000 Hz continuous sinus tone was calibrated with a sound level meter at 100, 90, 80, and 70 dB sound pressure level (SPL) for a matched pair of TDH-49 headphones. The calibrated tones will be cut into segments of 40 ms duration (10 ms rise/fall time) to be used in the intensity oddball tasks.
- Subjects were instructed to ignore tones and attend to a silent video (underwater scenes taken from the Discovery Channel—Planet Earth DVD) presented on a computer monitor (constrained to 6 X 4 inches). Subjects were tested on the film content following each experimental block.
- No responses were required from subjects during the EEG recordings.
- The intensity MMN task was performed in a single session after the completion of three EEG/ERP tasks required for a larger study. These tasks include (a) a resting EEG task, (b) a novelty oddball task, and (c) an intensity modulation task. Breaks were provided to subjects within and between tasks.

ERP Recording and Data Analysis

ERP Recording ERPs were recorded from 72 scalp sites (BioSemi), using an active recording reference composed of sites PO1 (common mode sense) and PO2 (driven right leg), and rereferenced to nose offline. Continuous data were exported to NeuroScan format using PolyRex (Kayser, 2003). A second degree polynomial highpass filter spanning the entire recording block was applied, which was shown to empirically outperform other highpass algorithms commonly used to reduce or eliminate DC drift (Kayser et al., in revision). Continuous EEG were blink corrected using a spatial, singular value decomposition (NeuroScan). Stimulus-locked epochs (700 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, 2006a), 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.

Current Source Density (CSD) ERPs were averaged for each stimulus intensity and condition (standard, deviant, and equiprobable). 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, 2006b; Tenke & Kayser, 2005).

CSD-PCA CSDs corresponding to Standard and Deviant trials and the Equiprobable block for all levels of intensity were submitted to unrestricted PCA derived from the covariance matrix followed by Varimax rotation of covariance loadings (Kayser & Tenke, 2003). Factor scores for the equiprobable block are shown in Figure 2. Factor scores for Standards and Deviants are shown in Figure 4. (All factors derived from this PCA shown in Blue)

A separate PCA was conducted on difference CSD waveforms (Deviant-minus-Standard) at each level of intensity. (Factors shown in Green)

Participants

Healthy adults (N = 33; 16 female; age = 32±9.1 yrs) with no history of psychopathology or neurological disorder, all right-handed (Edinburgh Handedness Inventory LQ=81.9 ± 18.0).

Fig. 2: Validation of Intensity Dependence of N1/P2

(Standard LDAEP – see Poster 64) Attended, Variable-long latency ISI
(Equiprobable Block – Current Study) Unattended, Fixed 500 ms ISI

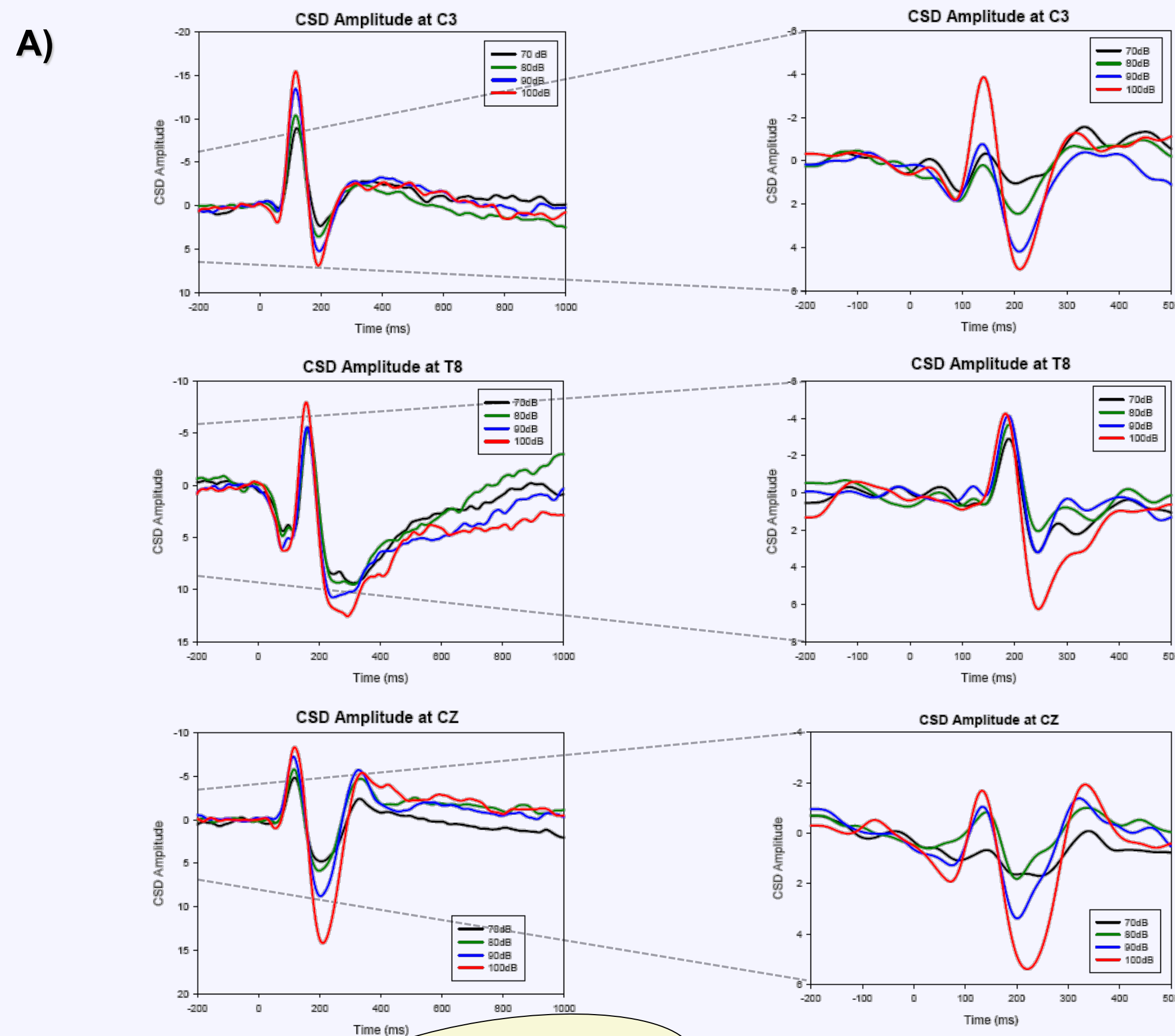
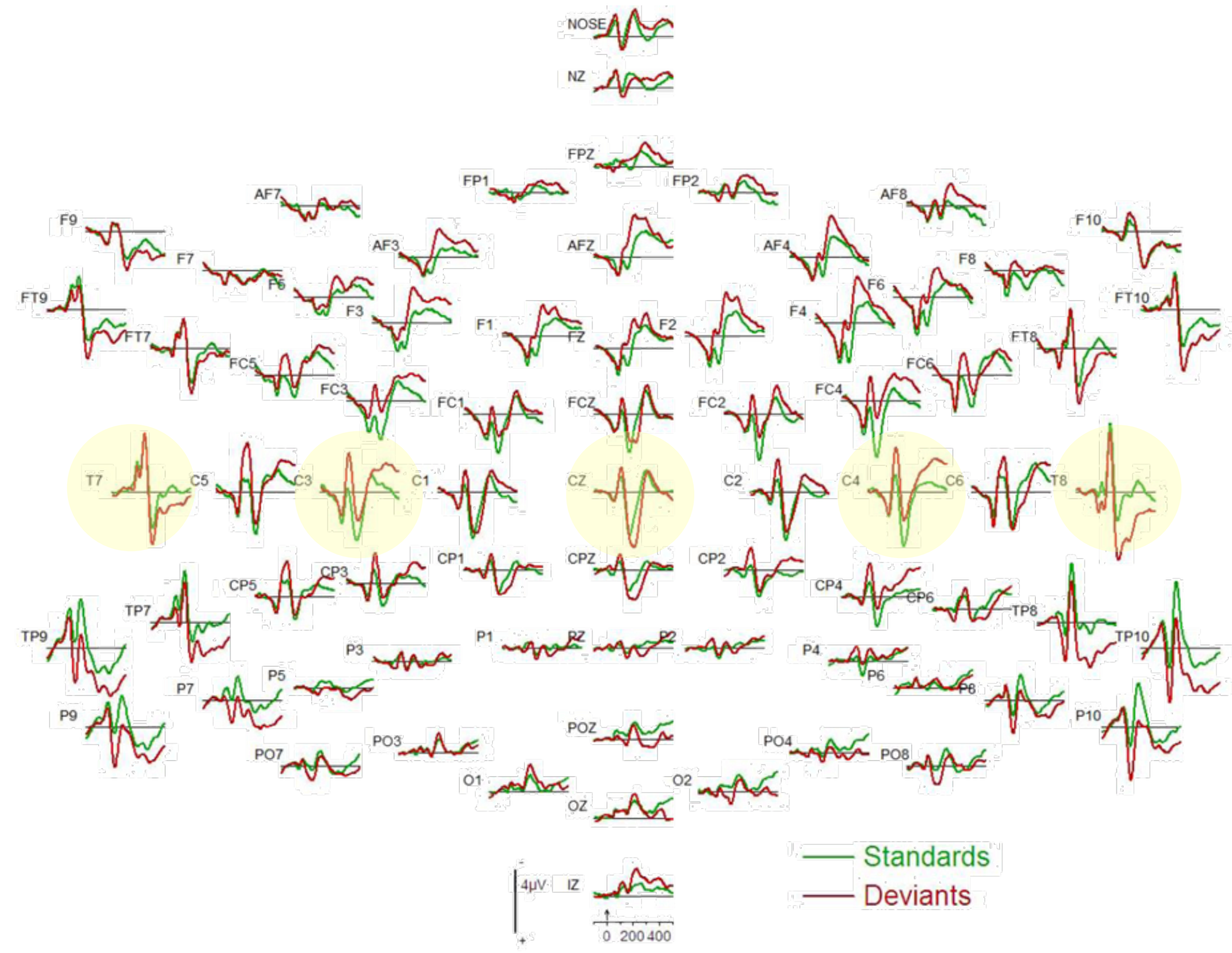
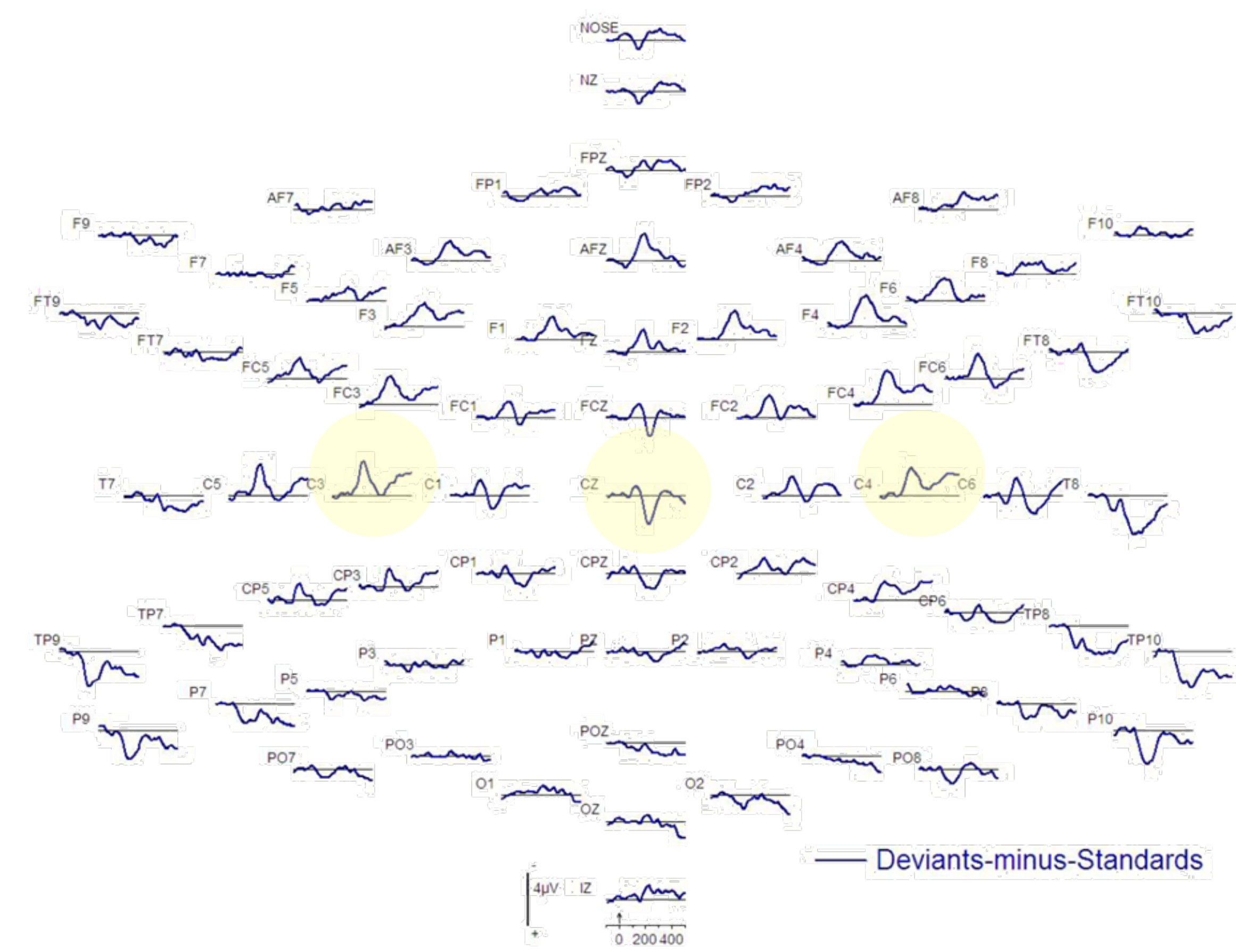


Fig. 3: Intensity MMN CSD Waveforms (Standard vs Deviant)



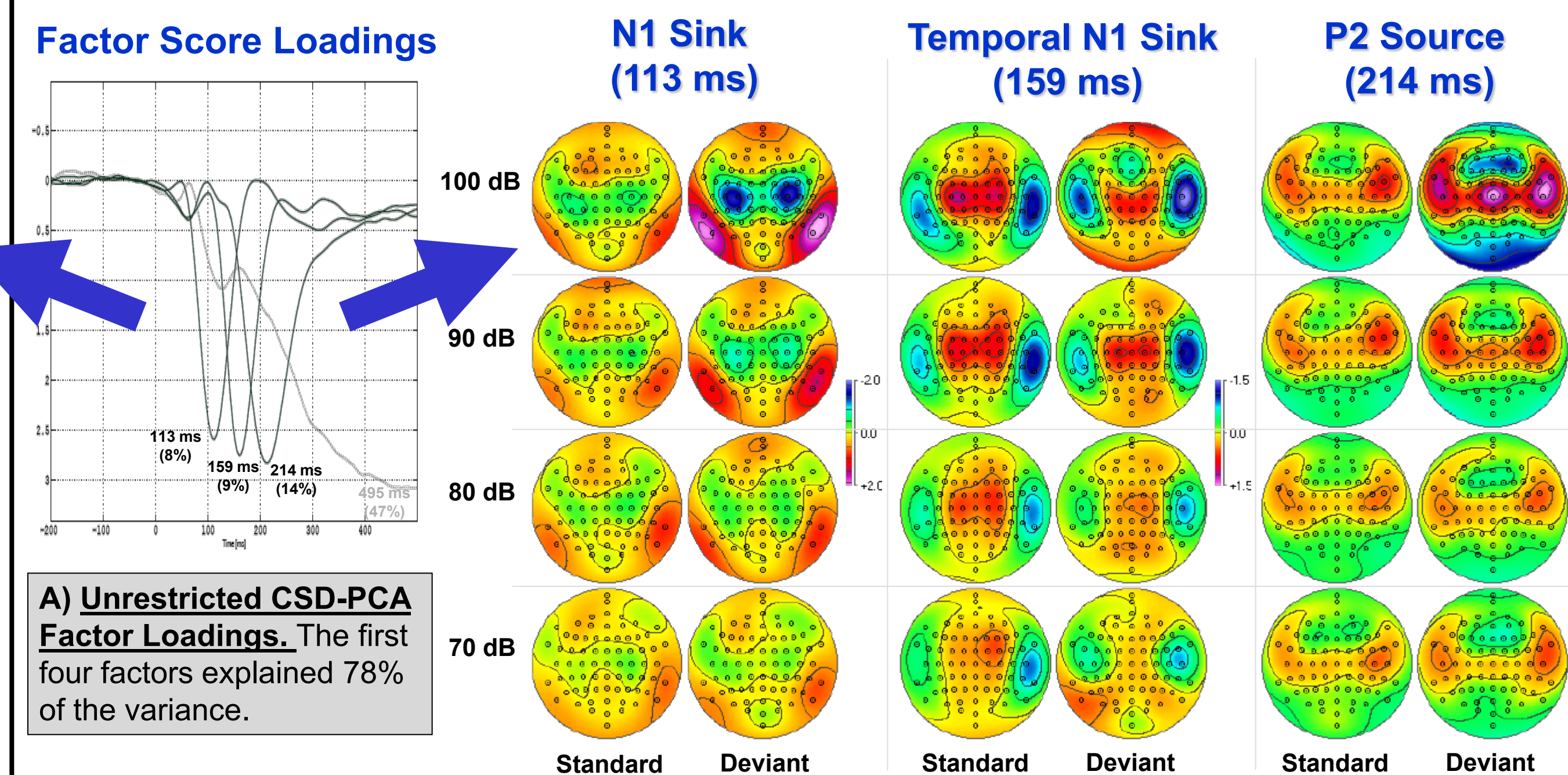
Grand Mean CSD Waveforms for Intensity MMN (Standards/Deviants) Task. Reference-free CSD waveforms show robust bilateral central sinks (C3/4; 113 ms), bilateral temporoparietal sinks (TP7/8; 153 ms) and bilateral central sources (C3/4; 214 ms) coincident with a midline source (CZ; 214 ms) across conditions.

Fig. 5: MMN Difference Waveforms (Deviant-Standard)



CSD Mismatch Difference Waveforms. Differential activity was seen at bilateral central sites (C3/4; 136 ms) stemming from enhanced sinks for deviants, which inverted at lateral temporoparietal sites (TP9/10), and included a large relative vertex source (230 ms).

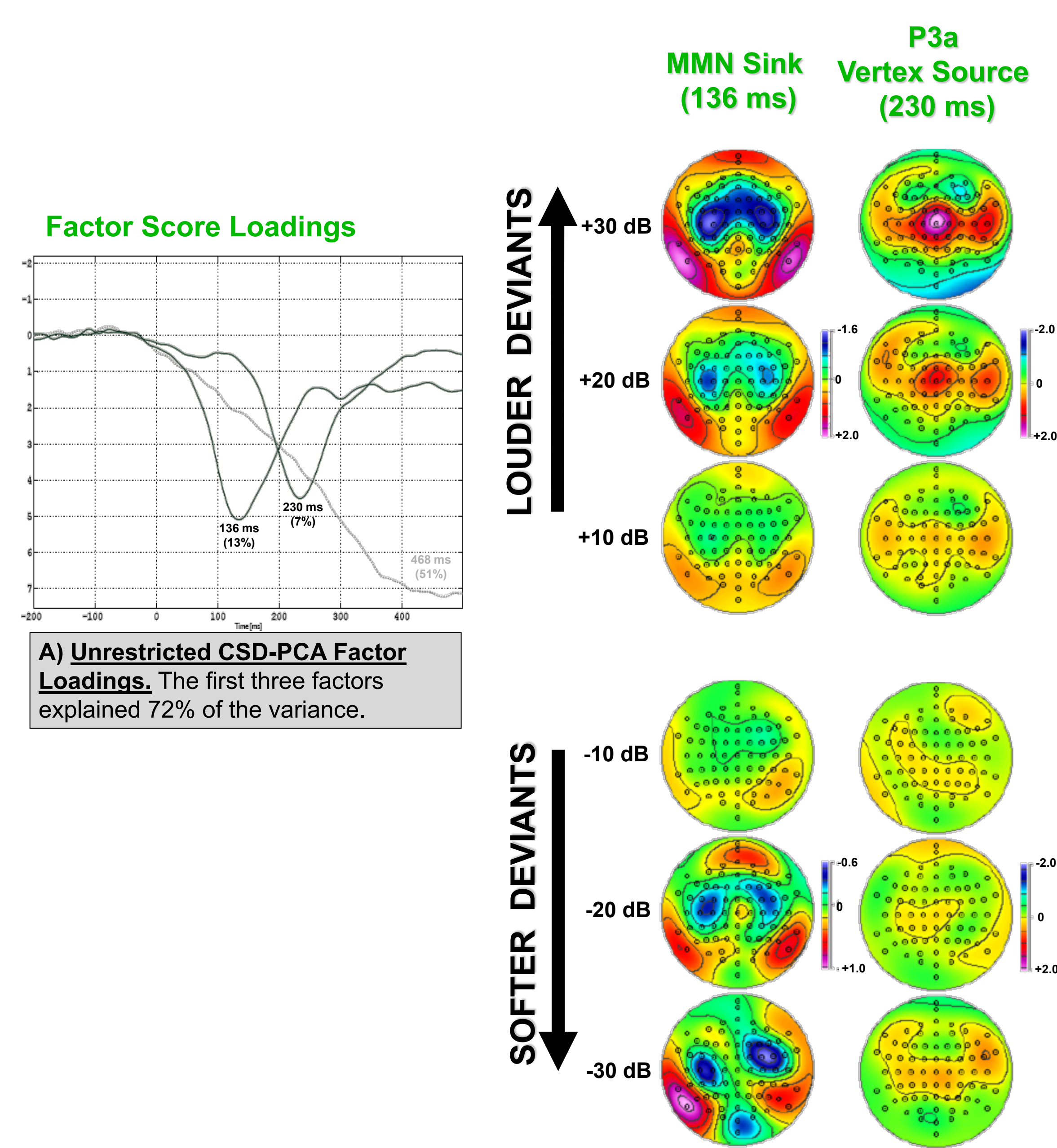
Fig. 4: CSD Factor Loadings and Scores for Standards and Deviants as Function of Intensity



A) Unrestricted CSD-PCA Factor Loadings. The first four factors explained 78% of the variance.

B) CSD-PCA Factor Score Topographies for Deviant and Standard Conditions at 100dB, 90dB, 80dB, and 70dB. Factor score topographies corresponding to N1 sink (113 ms), temporal N1 sink (159 ms), and P2 source (218 ms) showed a loudness dependency and were comparable for deviants and standards at most intensities differing primarily for loudest tone.

Fig. 6: CSD Difference Factor Loadings and Scores as a Function of Intensity



B) CSD Difference Factor Score Topographies for Intensity Disparity (+/- 10, 20, 30dB). Factor score topographies corresponding to a relative sink/source at 136 ms (MMN sink), reminiscent of N1 topography, and a relative vertex source at 230 ms (P3a) varied with the level of intensity disparity. While enhancements in both factors were observed to increases (+10...30dB) in the disparity of loudness between deviants and standards, MMN sinks were also enhanced for decrements (-10...30 dB) in intensity (Note different scaling for MMN sink between 'louder' and 'softer' maps).

References

- Gallinat, J., Bottlinger, R., Juckel, G., Munke-Puchner, A., Stotz, G., Kuss, H.J., Mavroggiorgou, P., & Hegerl, U. (2000). The loudness dependency of the auditory evoked N1/P2-component as a predictor of the acute SSRI response in depression. *Psychopharmacology (Berl)*, 148(4), 404-411.
- Hegerl, U., Juckel, G. (1993). Intensity dependence of auditory evoked potentials as an indicator of central serotonergic neurotransmission: a new hypothesis. *Biological Psychiatry*, 33(3), 173-187.
- 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 methodology for ERP component identification and measurement: theoretical rationale and empirical evaluation. *Clinical Neurophysiology*, 114(12), 2307-2325.
- Kayser, J., & Tenke, C. E. (2006a). Electrical distance as a reference-free measure for identifying artifacts in multichannel electroencephalogram (EEG) recordings. *Psychophysiology*, 43, 551.
- Kayser, J., & Tenke, C. E. (2006b). Principal components analysis of Laplacian waveforms as a generic method for identifying ERP generator patterns: I. Evaluation with auditory oddball tasks. *Clinical Neurophysiology*, 117(2), 348-368.
- Kayser, J., Tenke, C. E., Kroppmann, C. J., Fekri, S., Alschuler, D. M., Gates, N. A., Gil, R. B., & Bruder, G. E. (in revision). Current source density (CSD) old/new effects during recognition memory for words and faces in schizophrenia and healthy adults.
- Näätänen, R., Paavilainen, P., Alho, K., Reinikainen, K., & Sams, M. (1987). The mismatch negativity to intensity changes in an auditory stimulus sequence. *Electroencephalography and Clinical Neurophysiology*, 40, 125-131.
- Näätänen, R., Paavilainen, P., Rinne, T., & Alho, K. (2007). The mismatch negativity (MMN) in basic research of central auditory processing: a review. *Clinical Neurophysiology*, 118(12), 2544-2590.
- Perrin, F., Pernier, J., Bertrand, O., Echallier, J. F. (1989). Spherical splines for scalp potential and current density mapping. *Electroencephalography and Clinical Neurophysiology*, 72(2), 184-187. [Corrigenda EEG 02274, EEG Clin. Neurophysiol., 1990, 76, 668]
- Tenke, C. E., Kayser, J. (2001). A convenient method for detecting electrolyte bridges in multichannel electroencephalogram and event-related potential recordings. *Clin. Neurophysiol.*, 112, 545-550.
- Tenke, C. E., & Kayser, J. (2005). Reference-free quantification of EEG spectra: combining current source density (CSD) and frequency principal components analysis (fPCA). *Clinical Neurophysiology*, 116(12), 2826-2846.

Conclusions

Implications for Loudness LDAEP Literature

- Consistent loudness-dependency of N1/P2 was found for CSD-PCA factors derived from deviant, standard, and equiprobable CSD waveforms.
- Loudness-dependency of N1/P2 and intensity modulated MMN were shown in the same task using CSD-PCA.
- Although the standard LDAEP paradigm has been used to index the sensory response of auditory cortex (Hegerl & Juckel, 1993), overlapping preattentive processes (e.g., MMN, salience-detection) may contribute to its effects.

Relevance to MMN Literature

- MMN activity approximately spanned from 100 to 200 ms, overlapping factors corresponding to N1 sink and P2 source.
- As previously found, MMN varied with the size of the difference. While this effect was enhanced for louder stimuli, MMN was also observed for intensity decrements.
- These MMN findings are consistent with a preattentive deviance detection mechanism, but suggest that the mechanism is biased for more salient (e.g., louder) deviations in an established sensory pattern.
- For the loudest deviant (100dB) the MMN sink was followed by a P3a vertex source (coincident with temporal P2 sources) suggesting unique salience of this stimulus.