Title: Examining Inter-Trial Variability in, and Habituation of, Loudness-Dependent Auditory ERPs in Young Autistic and Typically-Developing Children

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Introduction: Autistic individuals often have atypical sensory experiences that are linked to anxiety (Green et al., 2012), adaptive functioning (Ausderau et al., 2016), activity participation (Little et al., 2015), and quality of life (Lin & Huang, 2019). The neurobiological underpinnings of these experiences remain somewhat unclear. Some (e.g., Haigh, 2018) postulate that increased endogenous neural noise might be responsible, which would be consistent with the hypothesis that excitation-inhibition imbalances decrease signal-to-noise ratios in autism (see Sohal & Rubenstein, 2019). There is also evidence to suggest that habituation to sensory stimuli might be reduced in autism and autistic sensory sensitivity (Green et al., 2015; Hudac et al., 2018). Using electrophysiology to identify the neural correlates associated with differences in autistic sensory processing may have important implications for intervention and accommodations to reduce the impact of sensory distress on autistic people’s lives. The present study investigates both habituation and random, inter-trial “noise” variability in a large dataset of auditory ERP responses collected as part of the Autism Phenome Project (APP).

Method: ERPs were examined in 130 young autistic participants (mean age = 38.50 months (SD = 6.02); mean MSEL DQ = 65.25 (SD = 20.91)) and 81 typically-developing controls (mean age = 37.09 months (SD = 6.46); mean MSEL DQ = 106.37 (SD = 11.58)). While watching a quiet video of their or a caregiver’s choice, participants heard, via headphones, brief complex tones randomly varying in loudness (50, 60, 70 or 80 dB SPL). 200-300 trials were collected in each loudness condition at an ISI randomly varying between 1-2s. 61-channel EEG was sampled at 1000 Hz, low-cut filtered offline at 0.4 Hz, and average-referenced. During data processing, Second-Order Blind source Identification (SOBI; Belouchrani et al., 1997) was used to remove non-neural noise. Epochs (-200ms to +599ms) were then high-cut filtered at 40 Hz (notch filter at 60 Hz). To examine habituation over the course of the experiment, linear slopes measuring change in amplitudes over successive trials were generated separately in each loudness condition, for every channel, and at every time-point between 0 – 350ms post-stimulus onset. Outliers were automatically excluded using Cook’s distance. To examine inter-trial noise variability, ERP waveforms in every trial were rescaled to be >0 through the addition of the greatest negative value as a constant to all values, after which coefficients of variation (median absolute deviations of amplitudes from all trials, normalized by the median trial amplitude) were generated separately in each loudness condition, for every channel, and at every time-point between 0 -350ms post-stimulus onset. Separately in each loudness condition, these habituation slopes and coefficients of variation were submitted to cluster-based permutation t-tests (Maris & Oostenveld, 2007) to investigate whether there were differences between ASD and TD.

Results: In 70 dB, the exploratory cluster-based permutation analysis revealed significantly more negative slopes in ASD over a variety of fronto-central channels from 226 – 350ms, p = .012, and significantly more positive slopes over a variety of posterior channels from 246 – 350ms, p = .03. In 80 dB, there were significantly more negative slopes in ASD from 81 – 350ms, initially over left fronto-temporal channels and then shifting to fronto-central channels, p = .003, and a more positive slopes over a variety of posterior channels from 96 – 243ms, p = .03. No effects of inter-trial random noise variability attained significance.

Discussion: While the present study’s finding of both increased and decreased habituation in ASD relative to TD may appear paradoxical, the apparent inversion of the slopes frontally and posteriorly may reflect the use of an average reference. If so, given the fronto-central and temporal topography of many auditory ERP responses, habituation slopes may be more positive in ASD for louder 70 dB and 80 dB sounds. Thus, autistic people’s sensory responses may show reduced habituation of a late fronto-central negativity (N2), and perhaps also a left temporal negativity (perhaps P1/Tb), but only in responses to loud sounds, not soft sounds. There was no evidence of differences between the ASD and TD groups in random inter-trial variability of ERP responses. This suggests that autistic sensory sensitivities at least in part reflect difficulties habituating to loud, ongoing sensory stimuli, rather than random variability in neural responses. Notably, in the present experiment, participants were not
instructed to attend to stimuli but were instead watching a movie of interest to them. Thus, the group difference in habituation might be caused by differences in the degree to which autistic people’s attention is captured by repeated, loud sensory stimuli.

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