RESEARCH ARTICLE

Increased Intra-Subject Variability of Reaction Times and Single-Trial Event-Related Potential Components in Children With Autism Spectrum Disorder

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Autism spectrum disorder (ASD) is an increasingly common neurodevelopmental disorder that affects 1 in 59 children. The cognitive profiles of individuals with ASD are varied, and the neurophysiological underpinnings of these developmental difficulties are unclear. While many studies have focused on overall group differences in the amplitude or latency of event related potential (ERP) responses, recent research suggests that increased intra-subject neural variability may also be a reliable indicator of atypical brain function in ASD. This study aimed to identify behavioral and neural variability responses during an emotional inhibitory control task in children with ASD compared to typically developing (TD) children. Children with ASD showed increased variability in response to both inhibitory and emotional stimuli, evidenced by greater reaction time variability and single-trial ERP variability of N200 and N170 amplitudes and/or latencies compared to TD children. These results suggest that the physiological basis of ASD may be more accurately explained by increased intra-subject variability, in addition to characteristic increases or decreases in the amplitude or latency of neural responses. **Autism Res** 2019, 00: 1–9. © 2019 International Society for Autism Research, Wiley Periodicals, Inc.

Lay Summary: The cognitive functions including memory, attention, executive functions, and perception, of individuals with ASD are varied, and the physiological underpinnings of these profiles are unclear. In this study, children with ASD showed increased intra-subject neural and behavioral variability in response to an emotional inhibitory control task compared to typically developing children. These results suggest that the physiological basis of ASD may also be explained by increased behavioral and neural variability in people with ASD, rather than simply characteristic increases or decreases in averaged brain responses.

Keywords: electroencephalography (EEG); event-related potentials (ERP); inhibition; emotion processing; intra-subject variability; autism spectrum disorder

Introduction

Studies assessing cognitive functions including memory, attention, executive functions, and perception, of individuals with autism spectrum disorder (ASD) often show inconsistent behavioral and neurophysiological findings [Happé, Ronald, & Plomin, 2006]. For example, no single cognitive task consistently elicits increased or decreased event-related potential (ERP) component amplitude and/or latency in children with ASD. However, increased intra-subject neural variability has been proposed as a potential objective and consistent marker of ASD [Baron-Cohen & Belmonte, 2005; Dakin & Frith, 2005; Simmons et al., 2009; Milne, 2011; David et al., 2016]. Accordingly, assessing both amplitude and latency of brain responses during cognition together with the variability of brain responses during cognition may provide a more complete characterization of atypical neurophysiological responses in ASD. Neural variability plays an essential role in functions such as plasticity, flexibility, perception, cognition, and behavior, as well as downstream effects of altered neural communication and connectivity [David et al., 2016]. Although some variability is necessary to perform these functions, too much neural variability can lead to reduced sensitivity of neurons, uncertainty, and ultimately, divergence from an idealized cognitive function [Masquelier, 2013; Caras & Sanes, 2019]. Neural variability can be divided into several distinct components, depending on the assessment tool being used. When recording with functional magnetic resonance imaging (fMRI), neural variability can be classified across space and separated into

"local" and "global" variability, whereas when using electro-encephalography (EEG), neural variability can be defined by deviation of ERP amplitude and latency responses to particular stimuli across individual trials [Milne, 2011; Dinstein, Heeger, & Behrmann, 2015].

Multiple studies have shown that individuals with ASD present increased intra-subject trial-to-trial variability measured by fMRI [Dinstein et al., 2012; Haigh, Heeger, Dinstein, Minshew, & Behrmann, 2015]. Specifically, children with ASD present abnormal neural activity in default mode brain areas that are not properly suppressed during certain tasks [Kennedy, Redcay, & Courchesne, 2006; Spencer et al., 2012; Hahamy, Behrmann, & Malach, 2015]. Nunes and colleagues also found that during rest, individuals with ASD show a more idiosyncratic organization of intrinsic connectivity networks, including the default mode and sensory motor networks, providing further evidence of increased ongoing neural variability in these particular neural regions in children with ASD [Nunes, Peatfield, Vakorin, & Doesburg, 2019].

Although fMRI provides excellent spatial resolution, the high temporal resolution of EEG makes it more ideal for time-based aspects of trial-to-trial variability analysis (i.e., accurately detecting variations in time-resolved neural responses to particular stimuli). One fMRI study assessing responses to sensory stimuli found increased intra-subject variability in individuals with ASD during a one-back task [Haigh et al., 2015]. Using EEG and steady-state visual evoked potentials, another study found reduced signal to noise in individuals with ASD [Weinger, Zemon, Soorya, & Gordon, 2014]. Only two studies have used EEG to examine neural variability through ERP amplitude and/or latency measures after visual, auditory, or tactile stimulation onset in individuals with ASD [Milne, 2011; Butler, Molholm, Andrade, & Foxe, 2017]. Milne found increased variability of the P100 component in these individuals, whereas Butler et al. reported no differences across groups on event-related spectral perturbations in somatosensory and visual ERPs. However, no study has assessed intra-subject variability of longer latency ERP responses.

A few studies have also shown that intra-subject reaction time (RT) variability has been used to predict cognitive performance, such that increased RT variability leads to reduced cognitive performance [Hultsch, MacDonald, & Dixon, 2002; Hultsch & MacDonald, 2012; Tamm et al., 2012]. This increased RT variability has been identified in individuals with ASD, irrespective of other comorbidities [Geurts et al., 2008; Milne, 2011]. Therefore, assessing both neural markers of variability (ERP amplitude and latency variability) together with behavioral markers (RT variability) would give us the unique opportunity to investigate a more complete picture of variability in ASD.

Neural and behavioral variability would provide a more cohesive explanation for a potential etiology underlying ASD rather than one particular cognitive deficit [Milne, 2011; Dinstein et al., 2012; Weinger et al., 2014; Haigh

et al., 2015]. The aim of this study was to identify behavioral and ERP variability differences between ASD and typically developing (TD) children on both inhibitory and face processing stimuli. We hypothesized that children with ASD would show greater variability in three measured modalities: RT, single-trial ERP component (N200, P300, N170) amplitude and latencies, and averaged amplitude over the time course of entire trials during a single emotional go/nogo task. Group differences in one of these measurements would advance our understanding of this phenomenon; however, observing greater variability over several measurements would provide a stronger argument for the field to investigate the nature of neural variability in ASD.

Methods

This article provides a new analysis of data previously reported by Magnuson et al. [2019] which showed reduced N200 component amplitude in children with ASD compared to TD children during a go/nogo task.

Data Collection

Data were collected during four single-day summer camps (methods adapted from Moreno et al., 2011), which involved research groups conducting behavioral and/or neurophysiological examinations of both children with and without ASD. Participants in groups of four to six were tested for 40 min in a large research room. For each participant, one experimenter explained and administered the task and one experimenter set up and administered the EEG scan. Written informed consent in accordance with the Declaration of Helsinki was obtained from each parent/guardian, and assent was obtained for each participant. The protocol was approved by the Office of Research Ethics at the Simon Fraser University (SFU).

Participants

Participants with ASD had a prior diagnosis of ASD from a qualified pediatrician, psychologist, or psychiatrist associated with the government-funded ASD assessment network or from a qualified private assessor in British Columbia. All diagnoses of ASD were based on the Diagnostic and Statistical Manual of Mental Disorders and confirmed using the Autism Diagnostic Interview-Revised and Autism Diagnostic Observation Schedule. Confirmation of the participant's diagnosis of ASD was provided by the parent in the form of a clinical diagnostic report or a Ministry of Child and Family Development ASD funding eligibility form. Over the course of the summer camps, 52 TD and 46 participants with ASD were recruited. Participants with ASD and a comorbid attention-deficit hyperactivity disorder (ADHD) diagnosis are

Table 1. Participant Demographics for Analysis of the N200, P300, and N170 Component Amplitudes and Latencies

ERP component at electrode location	Group	N	Sex (female participant count)	Age	IQ (WASI-II)	AQ	Comorbid ADHD
N2 at Cz (all trial types)	TD	30	9	9.6 ± 1.8	107 ± 10	15.5 ± 7.5	0
	ASD	25	5	10.0 ± 2.0	104 ± 18	31.2 ± 5.7	6
P3 at Cz (go trials)	TD	30	9	9.6 ± 1.8	107 ± 10	15.5 ± 7.5	0
	ASD	25	5	10.0 ± 2.0	104 ± 18	31.2 ± 5.7	6
P3 at Pz (nogo trials)	TD	30	9	9.6 ± 1.8	107 ± 10	15.5 ± 7.5	0
	ASD	25	5	10.0 ± 2.0	104 ± 18	31.2 ± 5.7	6
N170 at P3 (all trial types)	TD	30	9	9.6 ± 1.8	107 ± 10	15.5 ± 7.5	0
	ASD	19	3	10.1 ± 2.0	108 ± 17	30.4 ± 5.6	5
N170 at P4 (all trial types)	TD	30	9	9.6 ± 1.8	107 ± 10	15.5 ± 7.5	0
	ASD	24	5	10.0 ± 2.0	105 ± 17	30.9 ± 5.8	6

Note. The table shows group comparisons of sex, age, IQ, AQ, and comorbid-ADHD across groups.

common and therefore were included in the data analysis. ADHD diagnoses were determined through a parent report form. Individuals with comorbid intellectual disability (an IQ <70) were excluded from the study. Participants with less than 30 correct nogo trials were also removed from the analysis. Finally, due to the high intersubject variability observed in the superimposed ERPs of individual subjects, significant outliers, based on mean amplitude readings of 1.5× the interquartile range for the N200 and P300 peaks, were also excluded. After the exclusion criteria were met, 30 TD and 25 participants with ASD were retained for the N200 and P300 data analyses. From these participants, only extreme outliers, as characterized by mean amplitude readings of 3× the interquartile range, were removed for the N170 analysis in order to retain the maximum number of participants. On the testing day involving individuals with ASD, one of the EEG caps used had an electrical limitation—the P3 electrode was rerouted by the manufacturers to capture EOG signals. This specific cable placement was unchangeable. The experimental setup of this study requiring multiple participants to be tested at one time meant that one participant per group in the ASD pool of participants was tested using this cap, and therefore, data at the P3 electrode site were not obtained from these individuals. Participants were between the ages of 6 and 12 years, and no significant group differences were identified for age, sex, or IQ ($P > 0.05$; Table 1). IQ was measured using the Wechsler Abbreviated Scale of Intelligence (WASI-II).

Inhibitory Control Task

EEG measurements were recorded during a single computerized emotional go/nogo inhibitory response task (Fig. 1). In each trial, emotional faces (happy or angry) were presented in the center of a computer screen followed by the presentation of a shape (circle or square). Both shapes and faces were randomized. Participants were instructed to ignore the faces, to press the space bar when they observed a circle on the screen, and to not respond when they observed a square. Squares appeared
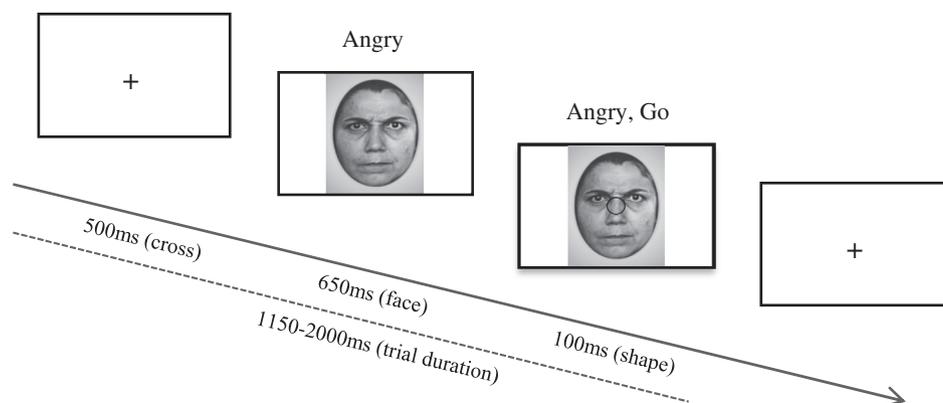

Figure 1. The stimulus display and its time course shown for the go/nogo task displaying the angry, go condition. After the presentation of the fixation cross, an angry or happy face is presented, followed by a circle or a square, to which the participant is either required to respond (circle) or inhibit a response (square).

in 20% of the trials, and circles appeared in the other 80% of the trials. Angry and happy faces each appeared 50% of the time. Participants received 60-sec breaks between every 100 trials. A maximum of 500 trials per participant were collected throughout the task. Participants practiced responding to 10 stimuli prior to task presentation. They were expected to achieve at least 80% accuracy on these trials before beginning the task.

EEG and Task Performance Data Acquisition:

The EEG data were recorded using eight-channel g.Nautilus EEG systems at the SFU Burnaby campus. ERPs were recorded from electrodes Fz, Cz, Pz, P3, and P4 at a sampling rate of 500 Hz. The EOG was monitored with two electrodes placed above and beside the left eye. A ground electrode was placed on the forehead, and a reference electrode was placed on the right ear lobe. Prior to the behavioral task administration, a resting state EEG measurement was recorded over a period of 3 min.

Behavioral Analysis

Mean accuracy across all trials and mean RT and intra-individual standard deviations of RT for correct go trials were calculated across all subjects. A total of 19% of the trials in the ASD group and 14% of the trials in the TD group were excluded from final analyses due to incorrect responses [Gonen-Yaacovi et al., 2016].

N200, P300, and N170 Variability Analysis

The data for all single trial analyses were low-pass filtered at 3.5 Hz, due to the strong influence of high-frequency noise on single-trial component amplitude and latency [Schürmann, Başar-Eroglu, Kolev, & Başar, 1995; Jaśkowski & Verleger, 2000; Blankertz et al., 2003; Saville et al., 2011]. The principle portion of the N200 and P300 are also largely low-frequency activity and, therefore, will not be greatly affected by a reduced low-pass filter. Trial epochs of 200 msec before the onset of the stimulus to 800 msec after the onset of the stimulus were obtained. Trials with significant eye movements and eye blinks were rejected based on a *z*-value cutoff of 6 obtained from average EOG. Trials containing components with peak amplitudes greater than 150 μV or less than −150 μV in the EEG channels Fz, Cz, Pz, P3, and P4 were also rejected. Group-averaged ERPs were calculated for trials on which participants responded correctly, with a 200 msec prestimulus baseline correction.

Intra-subject variability of the N200 and P300 amplitude was calculated by measuring the standard deviation of the mean voltage across trials within a predefined time window for each component at a given electrode. The N200 component typically peaks at approximately 200–300 msec poststimulus in adults and 300–400 msec poststimulus in children [Espinet, Anderson, & Zelazo, 2012; Brydges,

Anderson, Reid, & Fox, 2013; Shephard, Jackson, & Groom, 2014; Vuillier, Bryce, Szücs, & Whitebread, 2016]. Similarly, the P300 component typically peaks at approximately 300–500 msec poststimulus in adults and up to 600 msec poststimulus in children [Brydges, Fox, Reid, & Anderson, 2014; Rietdijk, Franken, & Thurik, 2014; Shephard et al., 2014]. The N170 component has also been shown to peak at later latencies (150–325 msec poststimulus) in children [Henderson, McCulloch, & Herbert, 2003; Moulson, Westerlund, Fox, Zeanah, & Nelson, 2009]. Therefore, based on the literature and a visual analysis of the group-averaged data, the latency window of interest for the N200 component was selected at 300–400 msec, 450–600 msec for the P300 component [Johnstone, Pleffer, Barry, Clarke, & Smith, 2005; Espinet, Anderson, & Zelazo, 2012; Vuillier et al., 2016], and 220–320 msec for the N170 component [Taylor, McCarthy, Saliba, & Degiovanni, 1999; Eimer, Holmes, & McGlone, 2003; Batty & Taylor, 2006]. The N200, P300, and N170 latency variabilities were calculated via standard deviation calculations of the time point of peak amplitude within the component's predefined latency window. For the N200 and P300 analysis, the central electrodes with the largest component amplitudes according to the group-averaged data were selected. However, literature consistently shows a maximal N170 component amplitude at temporal–occipital electrodes in both hemispheres during face processing, and, therefore, both the P3 and P4 electrode sites were used in the N170 analysis [Batty & Taylor, 2003; Hinojosa, Mercado, & Carretié, 2015]. Ongoing neural variability was estimated in a prestimulus interval (from −200 to 0 msec prior to go/nogo stimulus onset) and stimulus-evoked variability in a poststimulus interval (go/nogo stimulus onset to 500 msec poststimulus onset) across all correct trials [Gonen-Yaacovi et al., 2016]. This ongoing and stimulus-evoked neural variability was calculated by computing the variability within each time point within these latency windows and then averaging these variability measures to obtain an overall variance measure over the specified time windows.

Statistical Analysis

All data analyses were performed using SPSS, MATLAB, and the open-source Fieldtrip toolbox [Oostenveld, Fries, Maris, & Schoffelen, 2011]. A *P*-value less than 0.05 is received as statistically significant in the following analyses. A multivariate analysis of variance (MANOVA) was used to assess between-group differences of N200 and P300 component latency and amplitude variabilities and RT variability. Group was the between-participants factor and standard deviations of N200 and P300 amplitude and latency and RT, and artifact-free trial count were the dependent variables (methods adapted from Saville et al., 2011). These MANOVAs were performed for both go and nogo trials. Similarly, a MANOVA was used to calculate

Table 2. Mean and Standard Deviation Reports of Accuracy and Response Times of Go and Nogo Trials Across Groups (ASD, TD)

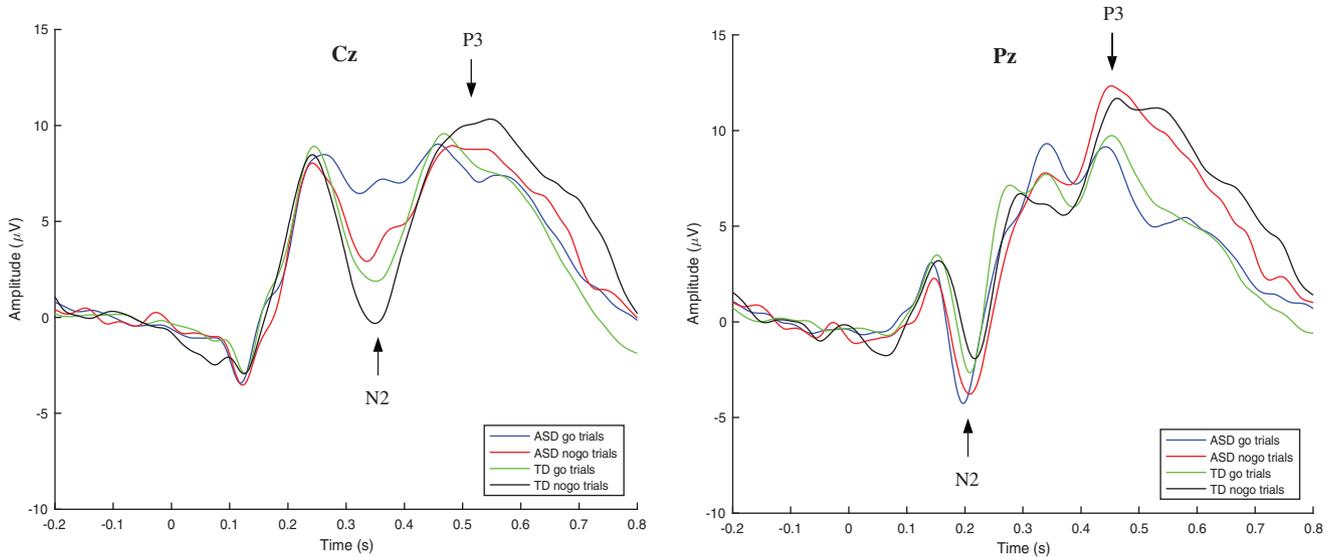| | TD (n = 30) | | | | | | ASD (n = 25) | | | | | |
| | RT (msec) | | Accuracy (% correct) | | Trial count | | RT (msec) | | Accuracy (% correct) | | Trial count | |
Dependent variable	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Go trials	405.8	52.1	89.5	9.7	234.4	47.1	405.1	99.2	86.7	11.5	221.0	52.8
Nogo trials	—	—	74.1	11.9	66.1	16.5	—	—	69.3	15.9	57.3	17.9

Figure 2. Grand-average go/nogo stimulus-locked waveforms for correct go and nogo trials in the TD and ASD groups at electrode site Cz (left) and Pz (right). Mean N2 and P3 component amplitudes were obtained from latency windows of 300–400 msec and 450–600 msec, respectively. N2-go, N2-nogo, and P3-nogo amplitudes were measured at electrode Cz, while P3-go amplitude was measured at electrode Pz.
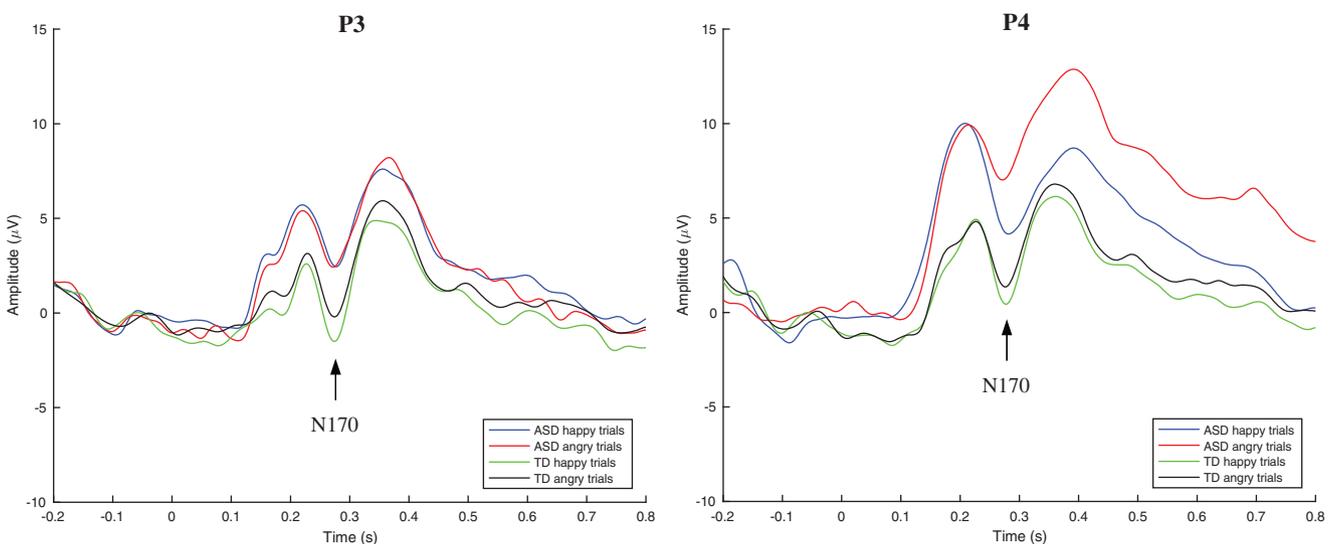

Figure 3. Grand-average face stimulus-locked waveforms for happy and angry trials in the TD and ASD groups at electrode site P3 (left) and P4 (right). Mean N170 component amplitudes were obtained from latency windows of 220–320 msec at both electrodes.

between-group differences of the N170 amplitude and latency variabilities, with artifact-free trial count included as well. Separate MANOVAs were used for the P3 and P4 electrode sites. These electrode locations were necessitated by the equipment limitations; however, typically posterior temporal–occipital electrode locations are used in N170 analyses [Batty & Taylor, 2003]. Across group differences for prestimulus and poststimulus ongoing and stimulus-evoked neural variability were calculated using independent-sample t-tests. Lastly, correlations between RT variability and N200-go and P300-go latency variability were calculated using Spearman's rho correlations.

Results

Intra-Subject RT Variability

Results from the MANOVAs showed greater RT variability across all correct go trials ($F(1,53) = 5.632$, $P = 0.021$, Cohen's $D = 0.61$) in the ASD group compared to the TD group. Reports of mean accuracy, RT, and trial counts and their standard deviations are shown in Table 2.

Intra-Subject N200 and P300 Variability

Group-averaged ERP waveforms are shown in Figures 2 and 3 for the N200/P300 and N170 components, respectively. The N200 and P300 amplitude and latency variability, and the ongoing and stimulus-evoked amplitude variability across trials are reported in Table 3. Results from the MANOVAs showed increased variability for the N200-go component amplitude ($F(1,53) = 4.332$, $P = 0.042$, Cohen's $D = 0.56$), the N200-go component

latency ($F(1,53) = 14.00$, $P < 0.001$, Cohen's $D = 1.02$), and the N200-nogo component latency ($F(1,53) = 5.295$, $P = 0.025$, Cohen's $D = 0.61$) in the ASD group compared to the TD group. No group differences were found for ongoing neural variability; however, the ASD group showed a trend toward greater overall stimulus-evoked variability within the poststimulus latency window of 0–500 msec, compared to TD individuals ($P = 0.084$; Cohen's $D = 0.47$). Lastly, a significant correlation between RT variability and P300-go latency variability was found across all subjects ($r_s = 0.307$, $P = 0.022$).

No between-group differences were found on the number of trials used for the N200 and P300 go and nogo analyses, suggesting similar error rates and artifact-free data across groups [Saville et al., 2011]. The percentages of trials lost were $6.3\% \pm 8.9\%$ in the ASD group and $8.3\% \pm 11.4\%$ in the TD group.

Intra-Subject N170 Variability

Group-averaged mean and standard deviation reports of the intra-subject trial-to-trial N170 variability are shown in Table 4. The MANOVA for the N170 component at the P3 electrode site showed increased variability for the N170 amplitude ($F(1,53) = 5.581$, $P = 0.022$, Cohen's $D = 0.63$) in the ASD group compared to the TD group. A large N170 amplitude variability in the ASD group at the P4 electrode was identified (Table 4); however, this appears to be driven by a single individual. No between-group differences on the number of trials used for the N170 analyses were identified [Saville et al., 2011]. The percentages of trials lost were $5.68\% \pm 7.22\%$ for the

Table 3.   Intra-Participant Variability (Standard Deviation) Across Trials of the N2 and P3 Component Amplitudes and Latencies

Dependent variables	TD amplitude variability (μV)	TD latency variability (sec)	ASD amplitude variability (μV)	ASD latency variability (sec)
N2 go trials	12.7 ± 2.4*	0.043 ± 0.002*	14.2 ± 2.9*	0.045 ± 0.002*
N2 nogo trials	13.7 ± 3.3	0.042 ± 0.003*	13.9 ± 4.0	0.044 ± 0.003*
P3 go trials	12.3 ± 2.9	0.063 ± 0.003	13.6 ± 3.2	0.064 ± 0.003
P3 nogo trials	13.8 ± 3.6	0.062 ± 0.004	13.8 ± 3.8	0.060 ± 0.006
Prestimulus (−200 to 0 msec)	12.5 ± 1.7	—	13.2 ± 1.6	—
Poststimulus (0–to 500 msec)	13.9 ± 1.8	—	14.8 ± 1.7	—

Note. Ongoing (−200 to 0 msec poststimulus) and stimulus-evoked (0–500 msec poststimulus) neural variability is also reported.
*$P < 0.05$.

Table 4.   Intra-Participant Variability (Standard Deviation) Across Trials of the N170 Component Amplitudes and Latencies

Dependent variables	TD amplitude variability (μV)	TD latency variability (sec)	ASD amplitude variability (μV)	ASD latency variability (sec)
N170 at P3 electrode	11.9 ± 2.4*	0.044 ± 0.003	14.9 ± 6.2*	0.045 ± 0.004
N170 at P4 electrode	11.8 ± 3.3	0.045 ± 0.003	35.8 ± 116.0	0.045 ± 0.004

*$P < 0.05$.

TD group, 8.44% ± 10.89% for the ASD group at the P4 electrode, and 8.43% ± 11.89% for the ASD group at the P3 electrode.

Discussion

This research extends established autism research paradigms and analytic approaches by investigating intra-subject neural variability with assessments of overall group differences in behavioral or electrophysiological responses as assessed in a previous study [Magnuson et al., 2019]. The results of the present study, which investigated three different variability measures, showed compelling evidence of increased behavioral and neural variability in children with ASD. Specifically, our results showed increased variability of the N200 amplitude and latency, N170 amplitude and latency, and RT responses in children with ASD compared to TD children. Although not significant, children with ASD also showed a trend toward significance for increased stimulus-evoked neural variability from 0 to 500 msec poststimulus. One limitation of the current study is the large N170 amplitude variability in the ASD group at the P4 electrode site driven by a single individual. This participant did not meet the exclusion criteria and, therefore, was not excluded from the analysis; however, after rejecting the participant, the standard deviation values in the ASD group become similar to the values in the TD group. Removing this participant does not change any of the main findings.

No study has identified a single mechanism underlying increased intra-subject variability in ASD; however, a number of theoretical accounts have been suggested including synaptic transmission and/or pruning abnormalities, irregular ion concentrations, and sensory gating impairments [Rubenstein & Merzenich, 2003; Dakin & Frith, 2005; Simmons et al., 2009]. Perhaps, the most common mechanism used to explain this increased neural variability in ASD is an imbalance of cortical excitation and inhibition, specifically increased glutamergic and/or reduced GABAergic signaling [Rubenstein & Merzenich, 2003]. Future studies should assess correlations between neural mechanism functions and neural variability in individuals with ASD.

Only two studies have previously assessed trial-to-trial neural variability using EEG in children with ASD [Milne, 2011; Butler et al., 2017]. In both of these studies, the average age of participants was 11–12 years. Butler et al. did not investigate behavioral responses, and Milne et al. did not find any differences in RT variability across groups. This is possibly due to compensatory neural mechanisms in the ASD group or a lack of neural/behavioral differences across ASD and TD individuals of this age. Milne and colleagues measured variability of early ERPs (P1), and Butler and colleagues employed a time–frequency analysis at the

single-trial level, measuring signal-to-noise ratios from 90 to 140 msec and focusing statistical cluster plot results on changes at 100 msec poststimulus for the visual response. Evidently, both studies measured early ERP component responses, and neither study assessed N200, P300, or N170 component amplitude and/or latency variability. Variability of these late ERP components provide a better reflection of higher order cognitive processes than exogenous components examined in these previous studies because these late components reflect dynamic processes involving continuously generating hypotheses about the stimulus, monitoring for conflict, producing responses, and allocating available neural resources to each given task [Dalebout & Robey, 1997]. The present study, therefore, provides further understanding into the behavioral and neural variability profile of children with ASD. The current study also found a relationship between brain and behavior as shown by a significant correlation between RT variability and P300-go latency variability.

Given the current findings of increased stimulus-evoked neural variability reflecting various cognitive processes, this study suggests that increased intra-subject variability in children with ASD is determined by a more continuous or global property of the central nervous system that is not confined to one particular cognitive deficit [Gonen-Yaacovi et al., 2016]. This global property could ultimately lend to perceptual difficulties and hypersensitivities/hyposensitivities in ASD [Dakin & Frith, 2005; American Psychiatric Association, 2013]. Interestingly, ongoing neural variability was not different across groups; therefore, the increased variability in individuals with ASD is specific to stimulus-evoked processes.

The results from Magnuson et al. [2019] show reduced neural responses to the inhibitory control task in the ASD group. This finding, paired with increased behavioral and stimulus-evoked neural variability in these children identified in the current study, warrants further investigation on the issue of whether reports of decreased brain activation from averaged ERP analyses might be the consequence of increased neural variability [Bender et al., 2015; Ouyang, Sommer, & Zhou, 2016]. More specifically, the study by Magnuson et al. [2019] reported reduced N200 component amplitude in children with ASD as compared to TD children. Thus, the increased variability in the N200-go and N200-nogo component latencies points to a possible underlying cause for the reduced N200 amplitude in this population. Although no causal links can be inferred [Di Russo & Spinelli, 2010], future studies with larger samples may explore such relations in ASD, given the evidence for increased intra-subject variability in these individuals [Milne, 2011; Weinger et al., 2014].

This is the first study to assess single-trial EEG neural variability of N170, N200, and P300 component latency, as well as ongoing neural variability and behavioral

(RT) variability in children with ASD. The methods and analyses used in the current experiment, and the results obtained from these analyses, showing increased neural variability in the ASD group, provide a robust measure of neurophysiological alterations underpinning cognitive difficulties in ASD. We believe our findings call for further investigations of single-trial ERP analyses in populations such as ASD, where increased intra-subject variability has been reported and inconsistencies across cognitive neural responses are present.

Acknowledgments

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