Vibrotactile sensory gating for diagnosing children with autism spectrum disorder and attention deficit hyperactivity disorder

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Abstract

Introduction: *Autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD) are neurodevelopmental disorders that can be observed from early childhood. The International Classification of Diseases 11th Revision (ICD-11) has introduced diagnostic criteria for atypical responses to sensory stimuli in ASD and ADHD patients. Therefore, to limit diagnostic errors and the number of qualitative methods used in diagnosing atypical sensory processing, it is essential to develop controlled experimental methods with standardised diagnostic thresholds that differentiate ASD, ADHD, and neurotypical (NT) children*

Methods: *Scalp electroencephalography (EEG) data were recorded from 53 ADHD, ASD or NT children (27 boys) aged 8–16 years during a sensory gating paradigm using vibrotactile stimuli on the fingertip. The sensory gating ratio, calculated as the mean amplitude of the N140 response between the first and second stimuli, was used to assess group adaptation to repetitive stimuli.*

Results: *The results showed significant differences in sensory gating between the three groups, even after controlling for age. However, post hoc tests revealed a significant difference only between children with ADHD and NT children. Additionally, significant differences were found in the amplitude of the N140 response to the second stimulus.*

Conclusion: *Sensory gating using vibrotactile stimulations shows potential for differentiating between ADHD and NT in older children. Future research should focus on exploring sensory gating of other event-related potential (ERP) components using vibrotactile stimuli.*

Keywords: Autism spectrum disorder, Attention deficit hyperactivity disorder, Sensory gating, Vibrotactile stimuli, Sensory processing, Event related potentials, Somatosensory evoked potentials

Introduction

ASD and ADHD are developmental disorders that can be observed from early childhood [22, 23]. In Denmark, ADHD occurs in 5.9% of children and adolescents, whereas ASD occurs in approximately 2.1% [1, 2]. Worldwide, ASD and ADHD co-occur in up to 80% of cases [25, 32]. Individuals with ASD and ADHD suffer from behavioural tendencies that challenge social interactions and interfere with school, work or other activities [22, 23]. A correct diagnosis is crucial, as different diagnoses require different interventions [6, 30, 13]. However, the diagnosis of ASD and ADHD relies on qualitative factors and observations of behaviour and responses [17, 9].

The ICD-11 changes how ASD and ADHD are diagnosed compared with the ICD-10 [31, 32]. Specifically, the ASD diagnosis now requires "Lifelong excessive and persistent hypersensitivity or hyposensitivity to sensory stimuli or unusual interest in a sensory stimulus..." [32]. Similarly, the ADHD diagnosis now requires "Easily distracted by extraneous stimuli or thoughts not related to the task at hand..." [32]. Parental reports have documented atypical sensory processing in both disorders, supporting the new ICD-11 criteria [20, 14].

Therefore, to diagnose correctly and limit the number of qualitative methods used in diagnosing atypical sensory processing, it is essential to develop controlled experimental methods with standardised diagnostic thresholds that differentiate ASD, ADHD, and NT children [17, 16, 6]. This leads to the question of how atypical sensory processing in children with ADHD and/or ASD might be measured.

Electroencephalograms (EEGs) are typically used to measure neural activity in pediatric populations because of their temporal resolution and simplicity

[12, 18]. The EEG measurement of neuronal activity during stimuli is called the ERP, which is commonly used in the examination of sensory processing [29, 19][p. 365-374].

ERP studies in sensory processing often focus on auditory or visual stimuli, despite the tactile sense being the earliest developed and most important sense in early development [5, 20, 4]. The tactile sense is the first sense with which children sense the world and detect affection, reassurance and attention [14, 3, 5, 4].

Sensory processing in ASD patients has been thoroughly studied, but have shown varying results, which are thought to be attributed to differences in the type of tactile stimulation, cohort characteristics and stimulus location [25, 26]. Compared with other types of tactile stimuli, vibrotactile stimulation is more comfortable and less stressful for the wearer [27]. Therefore, due to the pronounced tactile reactivity of children with ASD and ADHD, this study will focus on studies examining sensory processing using vibrotactile stimuli.

Few studies have examined sensory processing in children with ADHD or ASD using vibrotactile stimuli. A study, investigating neural markers of tactile sensory processing in 47 infants with ASD and ADHD, measured EEGs during a sensory gating paradigm using vibrotactile stimuli on the feet. The results indicated that reduced tactile neural repetition suppression of the alpha range (6–10 Hz) in infants increases the chance of developing ASD traits later in life. The study concluded that exploring the associations between neural repetition suppression in the tactile modality and ASD and ADHD is essential.[25]

Another study examined cortical responses to tactile stimuli in children with ASD and their associations with tactile reactivity. They recorded EEGs from 78 ASD and NT children aged 3-6 years during repeated vibrotactile stimuli with an inter-stimulus interval of 150 ms to the participants' left index and middle fingers. The results showed a shorter latency and smaller amplitude of the late-latency N140 SEP response in children with ASD, despite the expected changes in early- to mid-latency SEPs. Furthermore, they found no differences in sensory gating of early-latency SEPs. They hypothesised that alterations might emerge later in development.[12]

Sensory gating paradigms are used to study cognitive and perceptual processes through repetition suppression behaviour [24]. Sensory gating paradigms involve measuring the ERP during two repeated, identical stimuli separated by a set interval [21, 8]. Sensory gating paradigms do not rely on participants' behavioural responses, which makes them suitable for individuals who are unable to understand complex instructions and are replicable across all age groups.[24]

In summary, research indicates that sensory gating paradigms using vibrotactile stimuli, especially the N140 response, might be viable for ADHD and ASD children. Furthermore, no studies have tested sensory gating of the N140 response in children older than 6 years. Therefore, to find a method with a standardised diagnostic threshold to support the ICD-11, this study explores whether the sensory gating paradigm combined with vibrotactile stimuli can differentiate ASD, ADHD, and NT children.

Methods and Materials

Data

This study utilised data collected in a study conducted at Aalborg University by Daniel Skak Mazhari-Jensen and Sabata Gervasio. The data included EEG measurements during vibrotactile stimulation from 53 children (27 boys), of whom 18 had ADHD, 16 had ASD, and 19 had NT between the ages of 8 and 16 years. Each participant underwent two measurements. Additional measurements were taken if errors occurred, resulting in a total of 109 EEG measurements. The scalp EEG was measured using the g.tec Nautilus wearable headset for children, which offers a sampling frequency of 500 Hz with 32 channels with wet EEG electrodes [15]. The electrodes are placed following the 10–20 system, with an impedance level below 50 kΩ, and reference to the right earlobe. The EEG was measured during a sensory gating paradigm using vibrotactile stimuli applied to the participants' second digit finger on the nondominant hand. The vibrotactile stimuli were delivered via tactors by Engineering Acoustics Inc [11], which vibrated the skin for 50 ms at a frequency of 300 Hz. The sensory gating paradigm delivered 60 pairs of stimuli with a 500 ms inter-stimulus interval, and a randomised interval from 6 to 10 seconds was used between pairs of stimuli. The paradigm was conducted twice with a 2-3 min break in between for a total of 120 stimuli. The participants were instructed to sit upright and relax in a chair while they watched a movie during the measurement. The duration of one measurement was approximately 10 minutes. A transistor-transistor logic signal, which indicated stimuli onsets, was saved alongside the signal in a CSV file.

Preprocessing

Preprocessing procedures were conducted via MATLAB (version R2023b) and a MATLAB plugin called EEGLAB [10]. The datasets for each participant were combined to include all measurements for the given participant. Two measurements were excluded because they lacked stimuli onsets. Through EEGLAB, the data were high-pass filtered via a 1651-order high-pass Hamming windowed-sinc finite impulse response (FIR) filter with a cutoff frequency of one Hz to remove DC drift. Artifacts were removed via independent component analysis (ICA). Independent components (ICs) were automatically rejected if the EEGLAB plugin called "ICLabel" found above a 90% chance that the ICs were either muscle or eye artifacts. On average, 1.89 ± 1.58 ICs were rejected. The data were low-pass filtered via a 167-order low-pass Hamming windowed-sinc FIR filter with a cutoff frequency of 40 Hz. The channels were subsequently rejected if they were flat for more than 30 seconds or if they correlated less than 0.8 with surrounding channels in a moving time window. On average, 1.61 ± 1.02 channels were rejected. The rejected channels were interpolated via spherical spline interpolation, and the channels were rereferenced to the average of all channels. To ensure that both stimuli were included in each epoch, the data were epoched from -200 to 1200 ms relative to the onset of the first stimulus (S1), provided a second stimulus (S2) occurred within 600 ms. The 200 ms prior to S1 onset was used as a baseline. All epoched measurements from each participant were combined into a single data variable, with an average of 114.74 ± 15.42 epochs per participant.

Somatosensory Evoked Potential Analysis

The SEP analysis was conducted through a MATLAB script. The data from each participant was averaged across all epochs. Figure 1 presents three examples of the grand average of the preprocessed data from one NT, ASD and ADHD child.

On the basis of the previous studies, the channels above the sensory cortex contralateral to the stimulated region, which are channel C3 or C4 for the hands, were selected for analysis [12, 25, 28]. C4 was used as a default if no dominant hand was included in the participant information. Furthermore, a previous study has found a different distance between the cortical representation of the fingers in

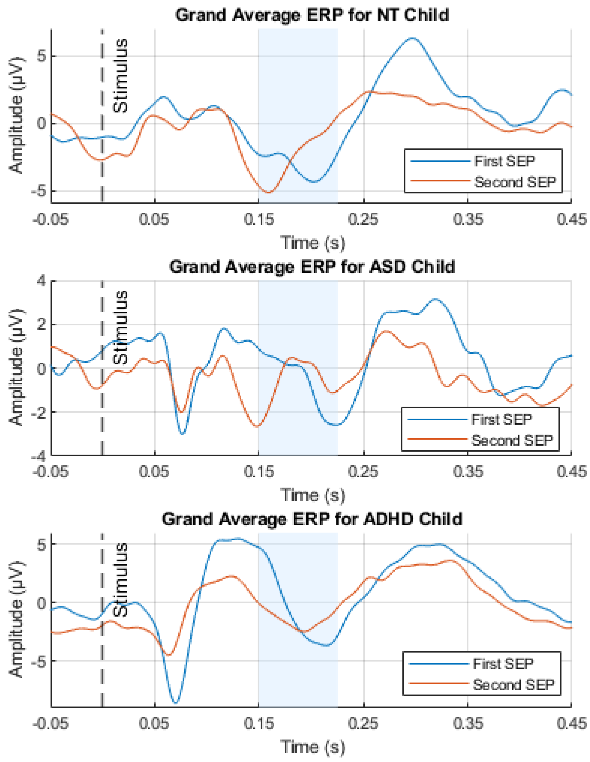

Figure 1: *This figure visualizes three subplots with the grand average of one NT, ASD and ADHD child. The stippled lines visualise the stimulus onset, and the blue area highlights the time window used to calculate the amplitude.*

ASD, suggesting that individuals with autism have an altered somatosensory cortex [7]. Therefore, the average signal from either C3 or C4 and their four neighbouring channels was used for analysis, which is a similar approach to literature [12]. Based on literature and visual inspection of the data, the N140 SEP response was identified as the most negative peak between 150 and 225 ms after stimulus onset [12, 28]. The ratio of sensory gating was determined based on the mean amplitude of N140. The mean amplitude was calculated by finding the area under the graph within 150-225 ms after stimulus onset [12]. The sensory gating ratio between the mean amplitudes of S1 and S2 was used for statistical analysis.

Statistical Analysis

Statistical analysis of the parameters was conducted via IBM SPSS Statistics. The purpose of the statistical analysis was to assess the difference in sensory gating between ASD, NT and ADHD children. One-way analysis of covariance (ANCOVA) was used for statistical analysis, with the sensory gating ratio as the dependent variable. A Sidak-corrected post-hoc test was conducted to detect significant differences be-

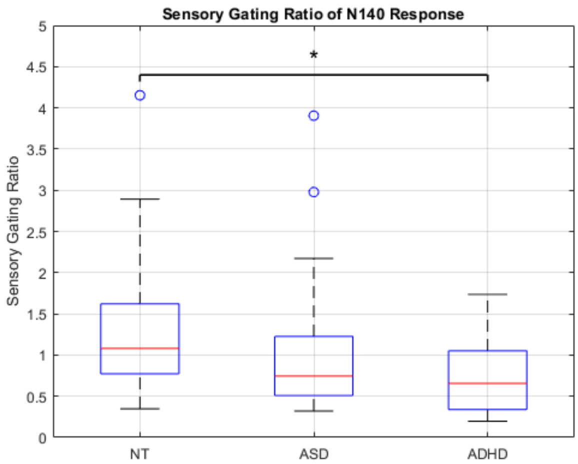

Figure 2: *Boxplot of the ratio between the amplitudes of the first and second stimuli of all the children in each group. The red line represents the median, and the blue box represents the values included between the 25th and 75th percentiles. The black lines represent the whiskers, which indicate the minimum and maximum values. The asterisk with the star at the top indicates a significant difference between the NT and ADHD groups.*

tween groups. As a secondary analysis, separate ANCOVAs were conducted to assess group differences in the N140 amplitude for S1 and S2. Age was used as a covariate in all ANCOVA tests, as studies have shown that it might affect the latency and amplitude of N140 [12, 28]. The dependent variables were tested for normality via the Shapiro–Wilk test. If the dependent variables were non-Gaussianly distributed, they were log-transformed prior to ANCOVA analysis. The significance level used was $\alpha = 0.05$.

Results

The purpose of this experiment was to examine whether ADHD, ASD and NT children could be differentiated by sensory gating. To assess this, the resulting sensory gating ratio for the N140 response from the three groups was visualised in a boxplot in Figure 2.

As seen in Figure 2, the three groups seem to overlap slightly, as they have similar minimums. The values of the median, 25th percentile, 75th percentile and maximum all decreased from left to right. The whiskers of the NT children ranged from approximately 0.4 to approximately 2.90. This range of the whiskers was almost halved in the ASD group, and the value of the ADHD group only ranged from approximately 0.25-1.75. Two outliers for ASD and one outlier for NT were presented as blue circles.

One-way ANCOVA was conducted to examine whether there were significant differences in sensory gating ratio between ASD, ADHD and NT in children, with age as a covariate. The analysis revealed a significant difference in sensory gating ratio between the combined groups, even after controlling for age, $F(2,48) = 3.804$, $p = 0.029$, η^2=0.137. The covariate had a negligible effect on the sensory gating ratio, $F(1,48) = 1.377$, p= 0.246, η^2=0.028. However, post hoc tests only revealed a significant difference between children with ADHD and NT children, p= 0.032. No significant difference was found between ADHD children and ASD children or between ASD children and NT children.

Additionally, separate ANCOVAs were conducted to examine whether there were significant group differences in the N140 amplitude of S1 and S2, with age as a covariate. A significant difference was found between groups in N140 amplitude of the S2, even after controlling for age, $F(2,48) = 5.058$, $p = 0.010$, η^2=0.174. Post hoc tests revealed a significant difference between ADHD and NT children, p= 0.011. Furthermore, the analysis found age-related differences on the N140 amplitude of S2, $F(1,48) = 13.177$, $p < 0.001$, η^2=0.215. No other significant differences were found.

Discussion

This project examined whether sensory gating could be used to differentiate ASD, ADHD and NT children. This project processed a scalp EEG dataset measured during pairs of vibrotactile stimuli on the fingertip. The sensory gating ratio of the N140 response was determined and analysed. One-way ANCOVA assessed that sensory gating significantly differed between the three groups, even after controlling for age. Post hoc tests revealed a significant difference between children with ADHD and NT children. Significant differences were found in the N140 amplitude of S2, even after controlling for age. Post hoc tests revealed significant differences between ADHD and NT children. Furthermore, age-related differences were found in the N140 amplitude of S2.

A study by Espenhahn et al. (2021), which examined vibrotactile stimuli applied to the fingertips, found no differences in repetition suppression among 78 children with ASD and NT children aged 3-6 years. They hypothesised that alterations in tactile sensory processing of children with ASD may develop at a later age.[12] Despite expectations, the current study found no differences in sensory gating between ASD and NT in older children. The lack of significant differences indicated that vibrotactile stimuli may be ineffective in differentiating ASD and NT children using sensory gating, as they share similar gating processes. However, a study by Piccardi et al. (2021) found reduced tactile neural repetition suppression of the alpha range (6–10 Hz) in infants increased the likelihood of developing ASD traits later in life [25]. The study by Piccardi et al. may yield different results compared to Espenhahn et al. and the current study due to methodological differences, the differences in the age of the participants, the limited number of participants in the current study, or the heterogeneity of the ASD diagnosis. The study by [25] stimulated the feet instead of the fingers, which could affect the result, as stimulating the feet evoked a different SEP signal at a different scalp location. Furthermore, they determined sensory gating based on the alpha frequency range rather than the amplitude.[25] This indicated that the use of the mean amplitude parameter in the current study and the study by [12] may be the cause of the different results. The mean amplitude is less robust to latency variation, as a varying latency peak might occur earlier or later than the set time window. However, the study by [12] found latency and amplitude differences in S1 using the mean amplitude with a similar time window (150-210 ms) to the current study (150-225 ms). The differences in time windows may reflect differences in the ERP signal between studies. Additionally, age have been found to affect the amplitude calculated in the time windows [28].

Despite the limitations of the mean amplitude calculation, the current study found significant differences in sensory gating and N140 amplitude of S2 between ADHD and NT children. The previously mentioned study by [25] found no significant differences in sensory gating in the alpha range using vibrotactile stimuli between ADHD and NT infants [25]. These results suggested that differences in sensory gating emerge in older children with ADHD. It could be discussed whether the differences in sensory gating occur due to decreased amplitude of S1. A decreased S1 amplitude would suggest that the individual has atypical sensory orientation and not sensory gating. Furthermore, on a physiological level, the N140 has been found to reflect attention and conscious perception of the tactile stimulus. Therefore, due to children with ADHD or ASD's atypical attention, it was expected that the amplitude of S1 may be decreased. However, the current study found significant differences in the N140 amplitude of S2 but not S1. This indicated that children with ADHD had atypical sensory gating of vibrotactile stimuli compared to NT children. It was expected that the typical sensory gating ratio would be between zero and one, as typical sensory gating should attenuate the amplitude of S2 compared to S1. Having a sensory gating above one indicated that the N140 amplitude of S2 is larger than S1, which was unexpected, especially in NT children. However, by visual inspection of the boxplot in Figure 2, the median value of the sensory gating of the NT children was above one. Furthermore, around 25% of both the children with ASD and ADHD had a sensory gating ratio above one. Therefore, the results suggested that most NT children and around 25% of children with ASD or ADHD suffer from heightened attention to repeated stimuli and dysfunctional sensory gating. It was expected that children with ASD or ADHD would have a sensory gating ratio around 1, which would reflect their atypical tactile reactivity. However, against expectations, the children with ADHD achieved a significantly lower sensory gating ratio than the NT, after controlling for age. These results may be due to previously mentioned limitations in the methods or limitations in the data used in the current study. The data in the current study included a limited number of participants, which increased the influence of outliers. Furthermore, there was no evaluation of the tactile reactivity of the participants. Therefore, the ASD or ADHD children may not suffer from atypical tactile reactivity, which has been found to affect early-latency ERP components [12]. Future research may investigate whether the tactile reactivity of the child influences the sensory gating of the N140 response. Subsequent studies may examine whether this difference in sensory gating might be used to assess the effectiveness of interventions.

Conclusion

Based on these findings, it is possible to differentiate between ADHD and NT in older children using sensory gating of the N140 response during vibrotactile stimuli. However, no significant differences were found between ASD and NT or ADHD children. Therefore, future studies should assess whether sensory gating differences can be found in other SEP components using vibrotactile stimuli.

Acknowledgements

This project was supported by supervisors Sabata Gervasio and Daniel Skak Mazhari-Jensen from Aalborg University in Denmark.

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