The Relationship Between Visual Evoked Potentials, Sleep, and Autistic Traits as Markers of Excitatory/Inhibitory Imbalance and GABAergic Functioning in Autism Spectrum Disorder

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Background

- Initial waveform peaks (i.e., N1 and P1) generated by visual evoked potentials (VEPs) represent early visual processing and reflect glutamatergic and GABAergic activity (*Figure 1*).
- Balanced excitatory and inhibitory (E/I) activity, driven by glutamatergic and GABAergic input, enables adaptive neural responses optimal for information processing.[1]

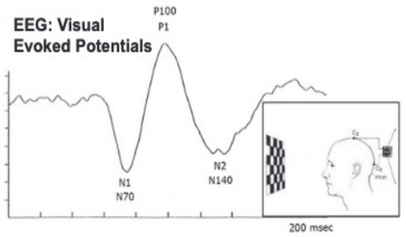

Figure 1. EEG recorded during a VEP paradigm and the resulting waveform.[1]

- In some individuals with autism spectrum disorder (ASD), E/I imbalance in critical neurocircuits leads to less efficient information processing.[2]
- Given GABA's role in sleep initiation and maintenance, high prevalence of insomnia and circadian sleep-wake rhythm disorders in ASD may be due to alterations in GABA-mediated processes.[3,4]
- **OBJECTIVE:** Compare (1) VEP P1 amplitude and latency and (2) sleep in autistic and neurotypical (NT) adults to evaluate (3) whether alterations in GABA-mediated processes explain variance in ASD traits.

Methods

PARTICIPANT CHARACTERISTICS

Table 1. Participant demographics; groups did not differ based on age or sex.

Participants	N (Female)	Age Mean (SD); Range	Full Scale IQ[a] Mean (SD); Range
ASD	40 (13)	27.4 (6.4) 18.0-39.5	110.4 (10.8) 84.0-129.0
NT	27 (16)	27.8 (4.8) 18.9-37.5	117.7 (15.6) 79.0-141.0

[a]Means significantly different between groups, p<.05

BEHAVIORAL AND COGNITIVE MEASURES

- ASD diagnoses were confirmed via the *Autism Diagnostic Observation Schedule* (ADOS-2) or the *Brief Observation of Symptoms of Autism* (BOSA) and clinician endorsement of DSM-5 criteria for ASD.
- Cognitive ability was assessed with the *Wechsler Abbreviated Scale Intelligence-II* (WASI-II).
- Subjective sleep quality was indexed using the self-report *Pittsburgh Sleep Quality Index* (PSQI), and autism traits were assessed using the self-report *Social Responsiveness Scale-2* (SRS-2).

EEG ACQUISITION AND ANALYSIS

- Electroencephalography (EEG) was used to record VEPs over the occipital cortex (O1, O2, Oz; *Figure 2*) during a pattern reversal checkerboard paradigm (*Figure 1*).
- Amplitude and latency of P1 peaks were extracted for analyses.

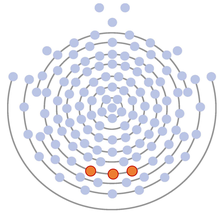

Figure 2. Occipital electrodes (O1, O2, Oz) on a 128-channel Hydrocel Geodesic sensor net.

STATISTICAL ANALYSIS

- Independent samples t-tests were used to compare group means of P1 amplitude and latency, sleep quality scores, and SRS-2 T-scores, and linear regression analyses were performed to examine the relationships between these variables.

Results

VEP P1 AMPLITUDE and LATENCY

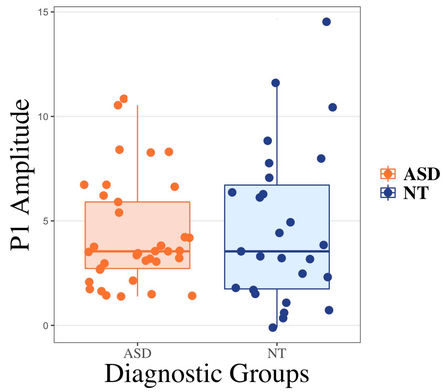

Figure 3. Distribution of P1 amplitude in ASD and NT adults (t(43)=-0.44, p=0.663).

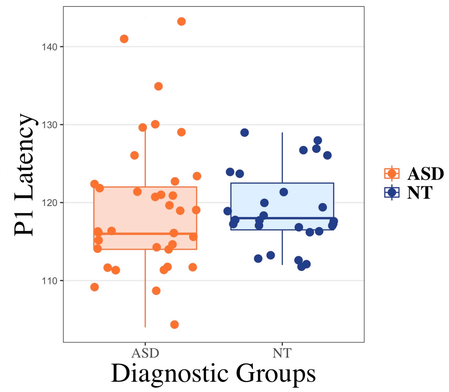

Figure 4. Distribution of P1 Latency in ASD and NT adults (t(59)=0.03, p=0.98).

- There were no significant differences in P1 amplitude (*Figure 3)* or latency (*Figure 4)* between diagnostic groups.

SLEEP

Figure 5. Distribution of PSQI Global Scores in ASD and NT adults (t(65)=4.43, p<0.001).

- Within ASD, increased PSQI global scores were associated with more autistic traits [SRS-2 total T-scores (*Figure 6*); SCI: (r(32)=0.46, p=0.007); RRB: (r(32)=0.35, p=0.041)].

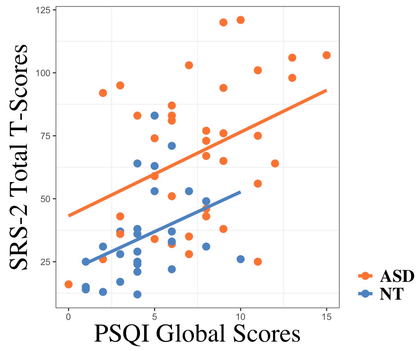

Figure 6. Positive associations between PSQI global scores and SRS-2 total T-scores in both the ASD (r(37)= 0.39, p=0.014) and NT (r(25)=0.37, p=0.055) groups.

- Compared to the NT group, adults with ASD endorsed poorer sleep via the PSQI with respect to global sleep quality (*Figure 5*), sleep efficiency scores (t(64)=2.29, p=0.026), sleep disturbance scores (t(49)=2.98, p=0.005), and sleep latency scores (t(55)=2.09, p=0.041).

ASD SYMPTOMATOLGY

- A significant P1 amplitude x diagnosis interaction for predicting SRS-2 total T-scores was detected (*Figure 7*), such that there was a trending positive association between P1 amplitude and autistic traits in the ASD group (F(1,34)=3.15, p=0.085) that was not present in the NT group (F(1,25)=2.32, p=0.139).
- In the ASD group, a positive association between P1 amplitude and SRS-2 SCI subdomain T-scores also approached significance (F(1,34)=3.39, p=0.074); this association was not observed in the SRS-2 RRB subdomain (F(1,34)=1.53, p=0.225).

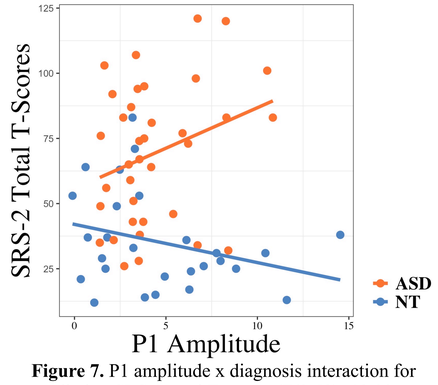

Figure 7. P1 amplitude x diagnosis interaction for predicting SRS-2 total T-scores (F(3,59)=13.09, p=0.024).

Results

ASD

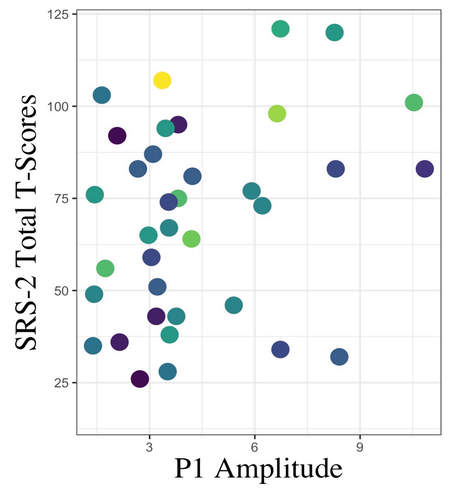

Figure 8. P1 amplitude x PSQI global score interaction for predicting SRS-2 total T-scores in adults with ASD (F(3,32)=2.96, p=0.262).

- No significant relationships were found between PSQI global scores and P1 amplitude in the ASD (F(1,35)=0.13, p=0.721) or NT (F(1,25)=0.49, p=0.488) groups.
- There was no significant P1 amplitude x PSQI global scores interaction for predicting autistic traits via SRS-2 T-scores in individuals with ASD (*Figure 8*).

Conclusions

- Consistent with previous literature, adults with ASD reported poorer sleep compared to neurotypical adults, which was also associated with more autistic traits.
- Contrary to previous findings, there was no difference in P1 amplitude or latency between diagnostic groups.
- However, increased P1 amplitude was associated with increased self-report of autistic traits within the ASD group but not the NT group, suggesting that differences in early visual processing, an index of E/I balance, predict more autistic traits for individuals with confirmed diagnoses of ASD.
- Although both overall sleep quality and P1 amplitude were associated with more autistic traits, these variables appear to impact SRS-2 T-scores independently within ASD.
- It is recommended that future research studies collect objective measures of sleep, such as polysomnography or actigraphy, to further probe these relations.

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