Developing the VEP task for clinical trial structure: factors that affect performance and test-retest reliability in children with ASD

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Background

- The core aim of the Autism Biomarkers Consortium for Clinical Trials (ABC-CT) is to identify biomarkers that can reliably measure treatment effects in autism spectrum disorder (ASD).
- This study focuses on analyses of Visual Evoked Potential (VEP) data collected during the EEG session across T1 and T2 time points (baseline and +6 weeks).
- The VEP paradigm aims to quantify low level visual processing in the visual pathway (occipital cortex to lateral geniculate nucleus to optic nerves) (Creel, 1990; Bonmassar, 1990).
- In the protocol, T2 visits were to occur 28-56 days after the T1 visit. However, 10.9% of the participants fell outside of the proposed T2 window range (19-80 days).
- Given that test retest reliability of the VEP (using ICC and presented at INSAR 2018) was .80 for the NT group and .68 for the ASD group, we examined protocol factors as potential moderators of the relation between T1 and T2 response.

Objectives

1) To evaluate factors that impact data acquisition and the VEP EEG biomarker N1 and P1 amplitude in participants with and without ASD.
2) Within the ASD group, how does autism severity impact data acquisition and validity.

Participants

- Participants were 225 6- to 12-years-old children (TD: n=64; ASD: n=161).
- Participants at 5 different sites viewed videos of flickering checkerboards with central red fixation point displayed for 500 msec while EEG was collected at baseline (T1) and at +6 weeks (T2).
- Five ABC-CT collaborating implementation sites:
  - Yale University
  - University of Washington
  - University of California, Los Angeles
  - Duke University
  - Boston Children's Hospital

Table 1. Participant characterization means and standard deviations

	ASD	TD
Participants	161	64
Age (years)	8.7 (1.6)	8.7 (1.8)
ADOS Calibrated Severity Score	7.6 (1.8)	1.8 (1.2)
DAS-II Full Scale IQ	95.7 (18.9)	114.6 (13.5)
# participants providing valid data (VEP) at both time points	115	54
# participants providing no data (VEP) at either time points	13	3
% out of window visits (19-27;56-80)	7.4%; 3.7%	6.2%; 7.8%

DAS-II = Differential Ability Scales-II
ADOS = Autism Diagnostic Observation Schedule

Procedure

- ABC-CT Main Study has includes EEG, Video Tracking and Eye Tracking. EEG always occurred in 1 session on day 2 of each time point.
- The EEG battery includes:
  - Resting Paradigm
  - ABCCT Faces Paradigm
  - Visual Evoked Potential (VEP) Paradigm
  - Biomotion Paradigm

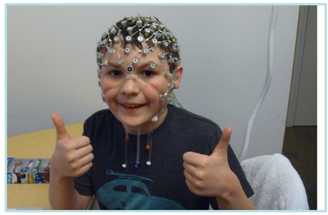
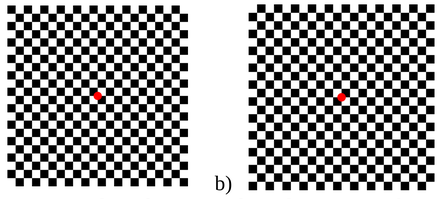


Figure 1. Participant wearing GSN-HydroCel-128 EGI cap for EEG data collection.

Stimuli

- Black and white checkerboard with central fixation that reverse their phase (Figure 1)
- Total of 100 phase reversals presented every 500ms.



a) b)

Figure 2. Screenshot of an image from the VEP paradigm (a) and (b) showing alternating checkerboards presented on screen.

Analysis

- EEG data quality inclusion criteria:
  - 60 attended and artifact free trials (from 200)
  - Visible / Quantifiable P1 peak
- Primary output variables include:
  - P1 and N1 amplitude across occipital midline region

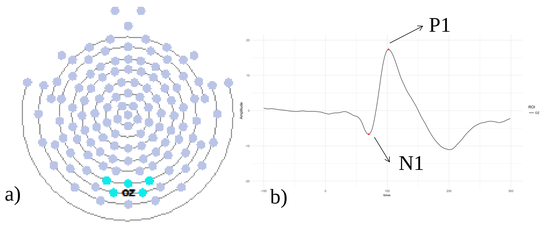


Figure 3. (a) VEP Analytic region of interest (ROI); (b) data output showing visible P1 and N1 peaks

Results

Do participants with ASD and TD perform differently in VEP data for the two points?

T1 VEP Valid Data Acquisition:
- ASD – 128/161
- TD – 55/64

T2 VEP Valid Data Acquisition:
- ASD – 135/161
- TD – 60/64

There was a group x timepoint effect, $\chi 2 = 3.883$ p=.05. Rates of data acquisition were similar at T1. At T2, more TD children provided data than ASD children.

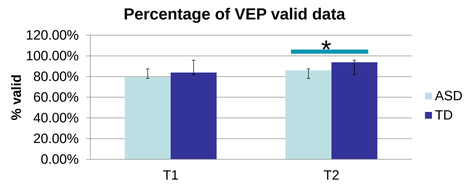


Figure 2. Diagnosis group differences in %Valid at T1 and T2

Does time of day and days between visits affect performance (number of good artifact free trials)?

- EEG time of day was similar across both groups and across two time points (T1: $\chi 2 = .579$, p=.447; T2: $\chi 2 = 3.33$, p =.19)
  - Coded as: AM (before 12pm); PM (after 12pm)

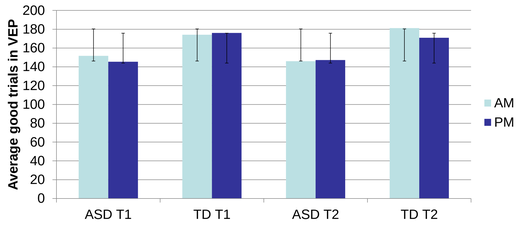
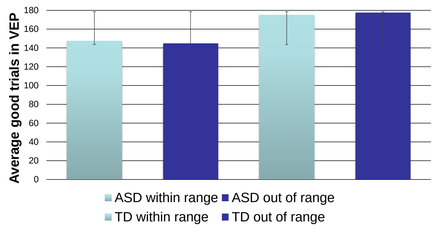


Figure 3. ASD and TD participants average good trials at different testing times (AM and PM)



- Days between T1 and T2 visits and whether participant provided valid data was not statistically significant (p=.69)

Figure 4. ASD & TD participants average good trials either within the expected range or outside of the expected time window. Within window (28-56 days); early out of range (19-27 days); late out of range (57-80 days)

Results Continued

Does ERP response at T1 predict T2 ERP response in the ASD group?

- Regression analysis shows that T2 ERP values were significantly predicted by both P1 and N1 amplitude at T1 in ASD group.
- ***P1: F=99.8, p < .001; N1: F=135.1, p<.001***

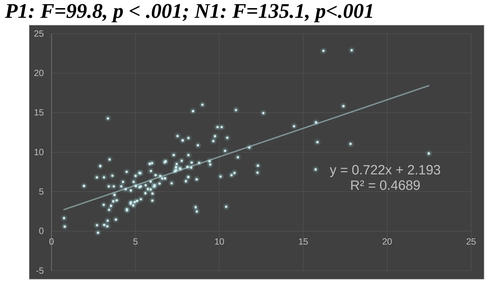


Figure 5. P1 amplitude in ASD group

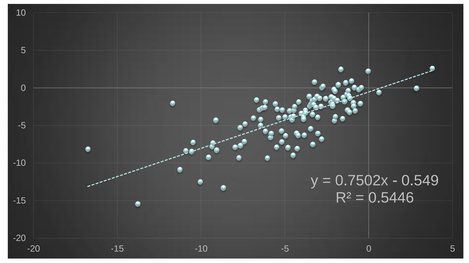


Figure 6. N1 amplitude in ASD group

Conclusions

- No significant differences were observed in time of day and time between visits across both diagnostic groups.
- ASD children did not perform differently at T2, suggesting that valid data can be acquired successfully at multiple time points which is beneficial in longitudinal clinical trials.
- TD children performed better and provided more data at T2 visit suggesting multiple exposure to EEG can lead to higher acquisition rates.

References

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