Developmental Differences in N170 Morphology in Children with Autism Spectrum Disorder: Results from the ABC-CT Interim Analysis

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BACKGROUND

- Individuals with autism spectrum disorder (ASD) exhibit increased latency of the N170, a face-sensitive event-related potential (ERP)
- The morphology of these ERPs is highly variable
- In 65% of typically developing (TD) children aged 4 to 12 years, the face N170 is *bifid* (i.e., shows two peaks; Taylor, Batty, & Itier, 2014)
- Variability in N170 waveform morphology has not been quantified across development in ASD or TD
- N170 morphology may reflect important underlying neural processes
- Understanding atypical waveform morphology and its relation to phenotype in ASD is necessary for understanding the potential of the N170 as a biomarker

OBJECTIVES:
1. Quantify bifid N170 morphology in children with ASD and TD controls
2. Quantify relationships among bifid N170 morphology, age, diagnosis, and clinical characteristics

METHOD

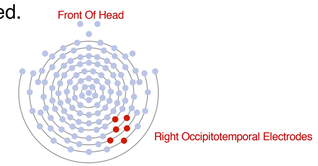
Participants:
- 172 children, 6 to 11 years of age, participating in the Autism Biomarkers Consortium for Clinical Trials (ABC-CT)

Behavioral Data:
- ASD diagnoses were confirmed via the Autism Diagnostic Observation Schedule (ADOS-2), the Autism Diagnostic Interview (ADI-R), and clinician endorsement of DSM-5 criteria for ASD
- Full Scale IQ (FSIQ): Differential Abilities Scale (DAS-II)
- Developmental Neuropsychological Assessment – Memory for Faces Subscale (NEPSY MF)

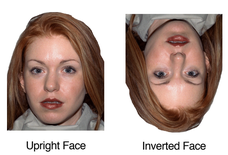
	n	Age	FSIQ *	ADOS CSS *	NEPSY MF *
TD	**57** (36 male)	**8.65** (1.73); 6.02 – 11.52	**114.40** (12.84); 88 – 150	**1.46** (0.73); 1 – 3	**11.26** (2.49); 6 – 16
ASD	**115** (88 male)	**8.76** (1.60); 6.07 – 11.50	**98.34** (18.18); 60 – 149	**7.64** (1.89); 4 – 10	**8.96** (2.87); 3 – 15

Presented as **Mean** (Standard Deviation); Range
* Means significantly differ between groups, $p < .001$

EEG Acquisition: EEG was recorded with a 128-channel HydroCel Geodesic sensor net. Right occipitotemporal electrodes were analyzed.



Stimuli: Upright and inverted faces and houses were presented. Upright and inverted faces were analyzed in the present study.

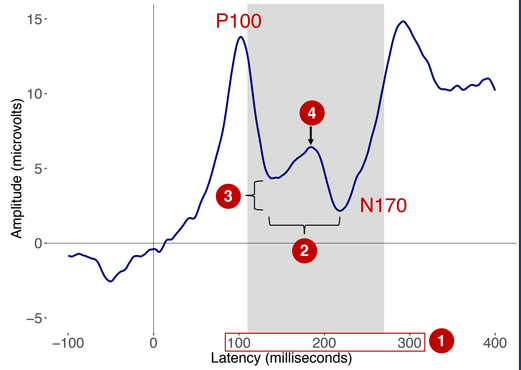


Statistical Analyses:
- Chi-square analyses were performed to determine the relationship between bifid N170 presence and diagnosis for both upright and inverted faces
- Logistic regressions were performed to determine the relationships between bifid N170 presence and age, N170 latency, and clinical characteristics for both upright and inverted faces
- For bifid N170 waveforms, the latency of the first negative peak was used in analyses

METHOD

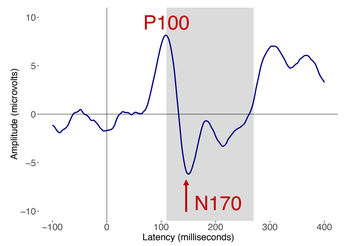
Bifid N170 Selection Criteria

1. Two negative peaks following a P100 between 100 and 300 milliseconds after stimulus presentation
2. Both negative peaks within 150 milliseconds of each other
3. Both negative peaks within 10 microvolts of each other
4. Negative peaks separated by a positive peak

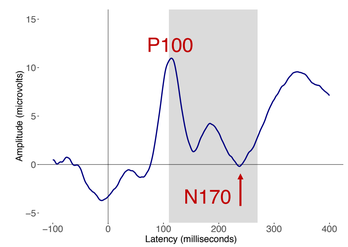


RESULTS

Examples of Variability in Individual Bifid Waveforms



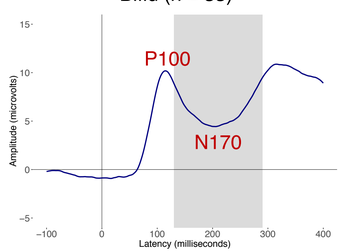
First negative peak is more negative



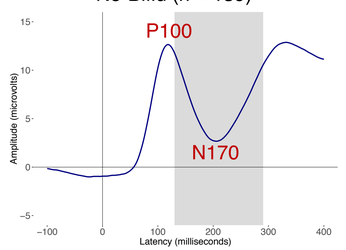
Second negative peak is more negative

Grand Average of Bifid Waveforms vs. No-Bifid Waveforms

Bifid (n = 33)



No-Bifid (n = 139)



Grand average of bifid waveforms reflects flattened peak and reduced negative amplitude (due to temporally separated negative peaks)

RESULTS

Bifid distribution among participants:
- There was no difference in bifid presence across diagnostic groups for upright faces (p = .700)
- Children with ASD were more likely to have a have a bifid N170 for inverted faces (p = **.026**)

Bifid Count	Upright Faces		Inverted Faces	
	Bifid	No Bifid	Bifid	No Bifid
TD & ASD	33	139	31	141
TD only	10	47	5	52
ASD only	23	92	26	89

Logistic regressions between bifid presence and age, clinical characteristics, and N170 latency for all participants:

TD & ASD	Upright Faces		Inverted Faces	
	B	*p*-value	*B*	*p*-value
Age	.001	**.032**	.000	.746
FSIQ	.002	.872	-.031	**.007**
ADOS CSS	.001	.980	.161	**.015**
NEPSY MF	.128	.064	-.106	.121
N170 Latency	-.050	**< .001**	-.028	**.006**

Logistic regressions between bifid presence and age, clinical characteristics, and N170 latency separated by diagnosis:

TD only	Upright Faces		Inverted Faces	
	B	*p*-value	*B*	*p*-value
Age	.001	.297	-.001	.370
FSIQ	-.015	.603	-.034	.400
ADOS CSS	-.134	.788	-.122	.857
NEPSY MF	.089	.539	.361	.113
N170 Latency	-.076	**.001**	.019	.272

ASD only	Upright Faces		Inverted Faces	
	B	*p*-value	*B*	*p*-value
Age	.001	.059	.000	.448
FSIQ	.008	.527	-.023	.082
ADOS CSS	-.073	.552	.135	.274
NEPSY MF	.183	**.036**	-.122	.128
N170 Latency	-.046	**< .001**	-.040	**.001**

DISCUSSION

- This is the first study to quantify bifid N170 morphology in TD and ASD children
- Bifid N170 morphology varied across individuals, which may yield less reliable N170 amplitude and latency estimates, and may affect grand averaged waveforms
- Overall, older age and faster N170 latency predicted bifid presence for upright faces, suggesting bifid morphology may reflect more efficient neural processing of faces in this constrained age range
- For inverted faces, lower cognitive functioning and greater ASD symptomatology predicted bifid presence, suggesting that these children processed inverted faces in a different way than upright faces
- In TD children, faster N170 latency only predicted bifid presence for upright faces, while in children with ASD, faster N170 latency predicted bifid presence for both upright and inverted faces
- In conclusion, our results indicate that waveform shape is meaningfully associated with individual variability within and between groups, which is relevant to interpreting ERPs as biomarkers in ASD
- Extant research, however, reduces this information to a single measurement, potentially discarding useful information about brain activity
- Approaches that quantify waveform shape may yield more informative representations of brain activity, but at the expense of simplicity
- Ongoing research focuses on analyzing the stability of bifid N170 morphology over time

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