The Relationship between Irritability and Neural Response to Faces in Autistic Children: Results from the Autism Biomarkers Consortium for Clinical Trials (ABC-CT)

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Background

- Prior literature has found prolonged P100 and N170 latencies to upright faces in autistic children relative to non-autistic children;[1] however, more research is needed to understand the heterogeneity in early face processing findings across studies.[2]
- Irritability, a transdiagnostic construct involving proneness to anger and low frustration tolerance, co-occurs in 10-25% of autistic individuals.[3]
- In studies conducted in non-autistic samples, adolescents with higher irritability had shorter N170 latencies to fearful, sad, and neutral faces,[4] while children with higher irritability had reduced P100 amplitudes to angry faces relative to neutral faces when controlling for anxiety.[5]
- Therefore, irritability may account for some of the individual differences observed in early face processing in autistic individuals.

Objectives

This research aimed to investigate relationships among irritability, P100 amplitude and latency, and N170 latency to faces and non-faces in a large sample of autistic children. It was hypothesized that higher irritability would predict:

1. shorter N170 latency to upright and inverted faces
2. lower P100 amplitude to upright and inverted faces
3. shorter P100 latency to upright and inverted faces

Methods

Participants

n (female:male)	Age in years (SD)	Full-Scale IQ (SD)	Irritability Z-Score (SD)
218 (54:164)	8.75 (1.61)	99.59 (17.65)	0.35 (1.08)

Table 1. Participant demographics.

- Data were collected from 280 autistic children during timepoint 1 of the Autism Biomarkers Consortium for Clinical Trials (ABC-CT).
- 218 participants were included in the current analyses (Table 1). Participants were excluded if a) a parent did not complete all questionnaires (n=4) or b) usable data was not collected during the Faces EEG experiment (n=58).

Clinical Measures

- All participants met diagnostic criteria for ASD and had IQs > 60.
- The *Aberrant Behavior Checklist (ABC)* and *Child and Adolescent Symptom Inventory, 5th edition (CASI-5)* are parent-report questionnaires that assess children's internalizing and externalizing symptoms and behaviors.
- Irritability symptoms were measured using age-normed Z-scores from the *ABC* irritability subscale. Generalized anxiety (GA) symptoms were measured using *CASI-5* GA T-scores.

Experimental Procedures

- Participants passively viewed three neutral female faces (upright and inverted) and three upright houses. 72 trials were presented for each stimulus type for a total of 216 trials (Fig. 1).

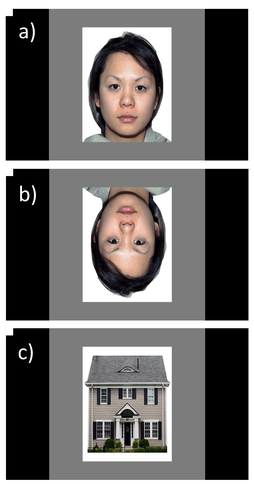

Figure 1. Trial stimuli. Examples of the trial stimuli, including a) upright faces, b) inverted faces, and c) upright houses.

Methods

EEG Acquisition and ERP Analysis

- EEG data were recorded at 1000 Hz with 128-channel EGI Hydrocel Geodesic sensor nets, processed, and segmented by trial. Data were averaged across the channels of interest (89, 90, 91, 95, 96) and across trials (Fig. 2).
- Peak amplitude and latency of the P100 and N170 were extracted using an automated algorithm and visually inspected for accuracy.

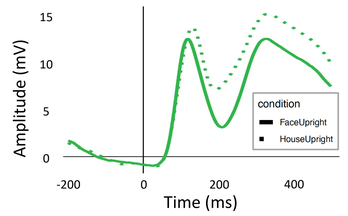

Figure 2. Grand average ERP waveforms to upright faces and houses.

Statistical Analysis

- Multiple linear regressions were performed to examine whether irritability symptoms predicted P100 and N170 amplitude and latency to faces and non-faces while controlling for anxiety symptoms[5] and age.[6]

Results: N170 Latency

- Higher irritability was marginally associated with longer N170 latencies to upright faces (Fig. 3b), while higher GA predicted significantly shorter N170 latencies to upright faces (Fig. 3c).

a) $N170_{latency} = 4.12*irritability_{Z\text{-}score} - 0.30*GA_{T\text{-}score} - 6.75*age_{years} + 287.76$

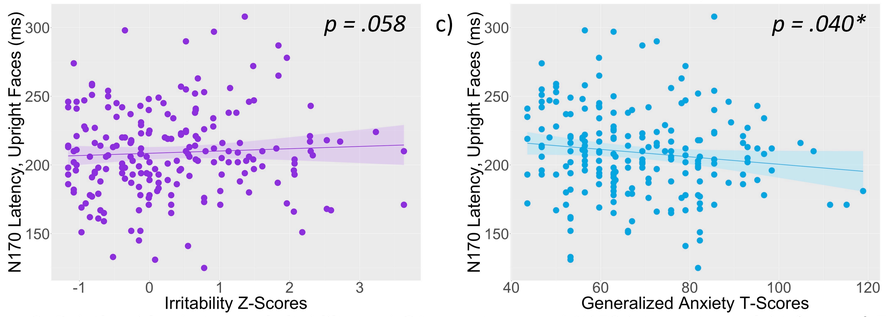

Figure 3. Relationships between irritability and GA symptoms and N170 latency to upright faces. a) The multiple linear regression model significantly predicted N170 latency to upright faces *(F*(3,203)=11.56, *p*<.001, R^2=13%). **b)** Children with higher irritability symptoms trended towards longer N170 latencies to upright faces (*b*=4.12, *SE*=2.16, *p*=.058). **c)** Higher GA levels predicted significantly faster N170 latencies to upright faces (*b*=-0.30, *SE*=0.15, *p*=.040).

- Children with higher irritability had significantly longer N170 latencies to inverted faces (Fig. 4b), while those with higher GA trended towards faster N170 latencies to inverted faces (Fig. 4c).

a) $N170_{latency} = 6.07*irritability_{Z\text{-}score} - 0.33*GA_{T\text{-}score} - 6.64*age_{years} + 275.87$

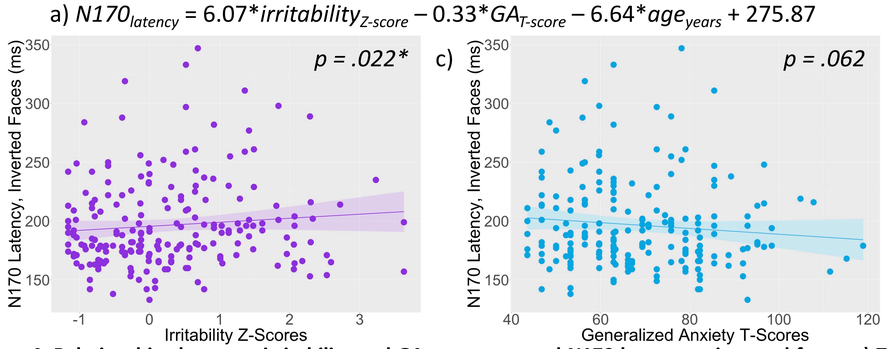

Figure 4. Relationships between irritability and GA symptoms and N170 latency to inverted faces. a) The multiple linear regression model significantly predicted N170 latency to inverted faces (*F*(3,202)=8.41, *p*<.001, R^2=10%). **b)** Children with higher irritability had significantly longer N170 latencies to inverted faces (*b*=6.07, *SE*=2.62, *p*=.022). **c)** Children with higher GA trended towards faster N170 latencies to inverted faces (*b*=-0.33, *SE*=0.18, *p*=.062).

Results: P100 Amplitude and Latency

a) $P100_{latency} = 1.04*irritability_{Z\text{-}score} - 0.17*GA_{T\text{-}score} - 3.67*age_{years} + 169.72$

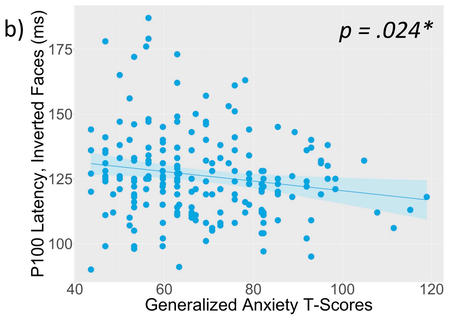

Figure 5. Relationship between GA symptoms and P100 latency to inverted faces. a) The multiple linear regression model significantly predicted P100 latency to inverted faces (*F*(3,203)=12.85, *p*<.001, R^2=15%). **b)** Autistic children with higher GA levels had significantly faster P100 latencies to inverted faces (*b*=-0.17, *SE*=0.07, *p*=.024).

- Irritability and GA levels were not significant predictors of P100 amplitude in any condition or P100 latency to upright faces (all *p*s>.10).
- Irritability was not significantly related to P100 latency to inverted faces (*p*>.10); however, children with higher GA had significantly faster P100 latencies to inverted faces (Fig. 5).

Conclusions

- Irritability and GA were associated with autistic children's neural responses to faces in distinct ways.
- Higher irritability was associated with longer N170 latencies to upright and inverted faces, contradicting hypotheses based on prior irritability research conducted with a non-autistic sample.
- In contrast, higher GA predicted shorter N170 latencies to faces. Higher GA was also associated with shorter P100 latencies to inverted but not upright faces.
- These findings suggest that autistic children with higher levels of anxiety may show more efficient processing of faces than autistic children with lower anxiety levels.
- Future research should consider the effects of co-occurring conditions when studying neural responses in autistic individuals.

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