Pivotal Response Treatment Increases Neural Processing Efficiency of Faces in Children with Autism Spectrum Disorder

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Background

Autism Spectrum Disorder (ASD) is a chronic neurodevelopmental condition characterized by a cluster of deficits in social communication and the presence of restricted and repetitive behaviors and interests.

Pivotal Response Treatment (PRT) is an evidence-based, naturalistic behavioral intervention derived from Applied Behavior Analysis. PRT targets "pivotal areas" of a child's development, domains in which improvement produces collateral gains in other areas not specifically addressed by the intervention.

- A 4-month course of PRT results in meaningful improvements in pragmatic language, social engagement, and adaptive functioning (Ventola et al., 2014)
- More normative neural responses in a biological motion perception task were observed following PRT, as indexed with fMRI (Ventola et al., 2015)
- To date, post-PRT changes in the temporal dynamics of neural activation have yet to be studied

The current study utilized event-related potentials (ERPs) to examine the temporal dynamics of social perception following a course of the PRT intervention

- P100 (P1)
  - Positive-going component recorded over occipital scalp approximately 100ms after viewing an image (Boutsen et al., 2006)
  - Believed to reflect processing of the low-level features of stimuli (Rossion & Caharel, 2011)
  - Amplitude modulated by attention (Herrmann & Knight, 2001)
- N170
  - Component with negative peak around 170 ms in the occipitotemporal regions
    - Peak is generally later in young children (Taylor et al., 2001)
  - Preliminary perceptual encoding of faces underlying categorization
  - When typically developing individuals view faces, the N170 component is of larger magnitude in the right hemisphere
- P300 (P3)
  - Large-amplitude positive component measured on parietal midline approximately 300ms after stimulus onset
  - Thought to reflect processing of information when it is incorporated into memory representations of the stimulus and context (Polich & Herbst, 2000)

We predicted that children would demonstrate improved social processing efficiency, as reflected in decreased latency of the N170 component, following a 4-month course of PRT. We also expect to see an increased level of processing of the stimuli, as indexed by an increase in the average P3 amplitude. These effects were expected to persist beyond the end of treatment. No changes in P1 amplitude or latency were expected.

Method

Participants:

- 7 children 4-6 year of age with ASD receiving PRT
  - Subset of 3 served as waitlist control (WLC) prior to enrollment in treatment
  - Artifact-free data was successfully collected from 5 out of the 7 children at a follow-up evaluation 16 weeks after the end of treatment
- Received PRT for 16 weeks
  - 8 hours per week (6 hours with the child and 2 hours of parent guidance)

Experimental Paradigm:

- Participants viewed computer-generated faces showing neutral and fearful affect
  - Attentional task (button press upon seeing bouncing ball) interspersed between trials
- EEG recorded at 4 time points:
  - Waitlist Control
  - Pre-Treatment
  - Post-Treatment
  - Follow-Up (16 weeks after treatment end)

EEG Data Acquisition and Collection:

- Recorded at 500 Hz
- 128-channel Hydrocel Geodesic Sensor net

	WLC	Pre	Post
Age	5.7 (0.62)	5.6 (0.91)	
DAS-II	112.3 (7.8)	112.3 (11.4)	
ADOS	17.3 (3.2)	17.9 (6.5)	12.4 (5.4)

Table 1: Group Statistics: Subject Age, ADOS severity score and IQ (DAS-II GCA) at waitlist (N = 3), pre-treatment (N = 7), and post-treatment (N = 7)

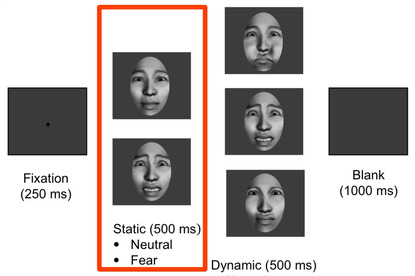

Figure 1: Experimental Paradigm. Static neutral or fearful faces were presented for 500 ms before they dynamically shifted into a different facial expression. ERP data was segmented to the onset of the static face.

Method

Statistical Analysis:

- Peak amplitude and latency of P1/N170 and average amplitude of P3 were analyzed using repeated measures ANOVA
- 2 within-subjects factors:
- Treatment (Pre/Post)
- Emotion (Fear/Neutral)
- Left-hemisphere and right-hemisphere N170 components were analyzed individually (LN170 and RN170, respectively)
- Paired samples t-tests for Waitlist Control vs. Pre and Follow-up vs. Post conditions

ERP Analysis:

- Data segmented to static face presentation within larger dynamic face paradigm
- Component statistics derived from average values across all electrodes in a particular cluster and time window
  - P1 window: 80-150 ms
  - N170 window: 164-290 ms
  - P3 window: 250-390 ms

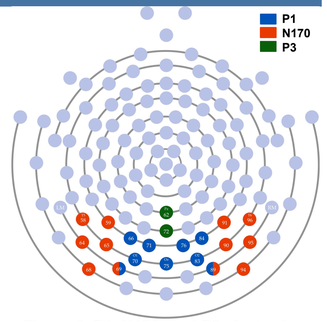

Figure 2: **P1, N170, and P3 electrode recording sites.** Data were averaged across all electrodes in each cluster (P1, Left N170, Right N170, P3)

Results

Post-Treatment

P1

- No significant effects on P1 amplitude (all F's < 1.16, p's > .324)
- Significant treatment effect on P1 latency [$F(1, 6) = 7.269$, $p = .036$, $\eta^2_p = .548$], qualified by a significant treatment x emotion interaction [$F(1, 6) = 6.422$, $p = .044$, $\eta^2_p = .517$]
  - Reduction in P1 latency with treatment was significant for neutral faces ($p = .021$) but not fearful faces ($p = .495$)

N170

- A main effect of treatment [$F(1,6) = 6.34$, $p = .045$, $\eta^2_p = .514$] indicated a change in face processing efficiency following PRT treatment, indexed by right-hemisphere N170 latency
  - Reduction in RN170 latency following treatment only trended toward significance for either neutral ($p = .065$) or fearful ($p = .092$) faces alone
  - No similar effect found in the left-hemisphere N170 latency ($p = .160$)
- Left-hemisphere N170 peak amplitude was significantly reduced from pre- to post-treatment [$F(1, 6) = 14.217$, $p = .009$, $\eta^2_p = .703$], reflecting an attenuated response in the hemisphere not typically associated with face processing
  - Significant for both fearful ($p = .039$) and neutral ($p = .008$) faces alone
  - There was no effect of treatment on RN170 peak amplitude ($p = .311$)
- No significant effects of emotion or emotion * treatment interactions on N170 amplitude or latency (all F's < .88, p's > .382)

P3

- No significant effects of treatment, emotion or emotion * treatment interactions on P3 average amplitude (all F's < .62, p's > .459)

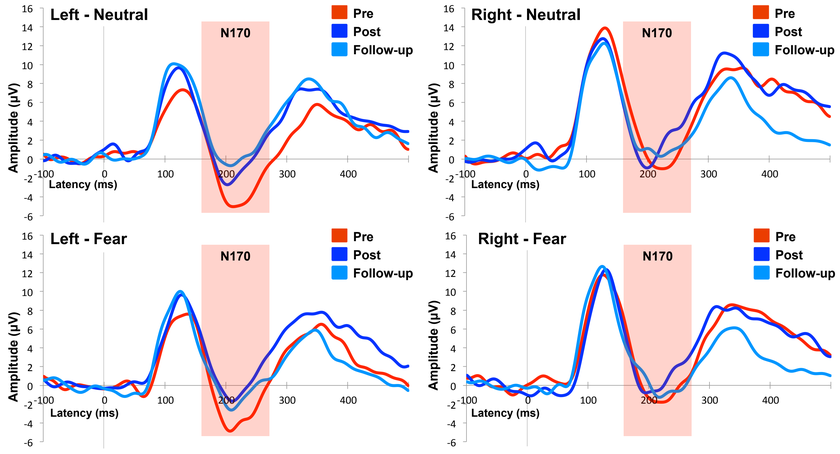

Figure 3: Grand average waveform depicting the Left and Right N170 across all participants (N= 7, N=5 for follow-up) for fear and neutral faces, at pre-treatment, post-treatment, and 16-week follow-up

Results

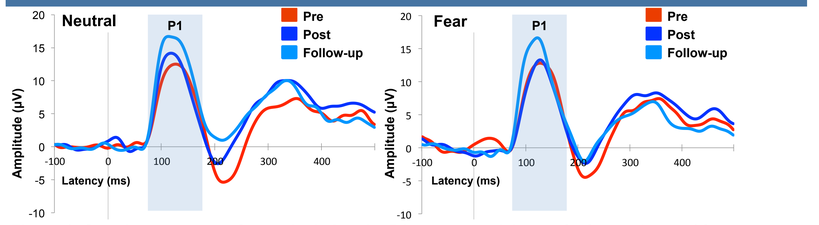

Figure 4: Grand average waveforms depicting the P1 across participants for fear and neutral faces, pre-treatment, post-treatment and at follow-up

Follow-Up

- Subset of 5 children
- Reduction LN170 peak amplitude did not change significantly 16 weeks post-treatment ($p = .454$)
- RN170 latency showed a marginally significant increase from post-treatment to follow-up ($p = .071$)
  - Latency increase was not significant for either fear ($p = .112$) or neutral ($p = .555$) faces alone
- P1 latency also did not differ between post-treatment and follow-up ($p = .104$)

Waitlist Control (WLC)

- Subset of 3 children
- P1 latency showed marginally significant increase over waitlist control period ($p = .087$)
- No significant change in RN170 latency across waitlist period for either emotion (p's > .123)
- LN170 peak amplitude was increased over the waitlist control period when children viewed fearful ($p = .017$) but not neutral ($p = .322$) faces
- No significant changes in P1 amplitude, LN170 latency, RN170 amplitude, or P300 average amplitude over this period (all p's > .213)

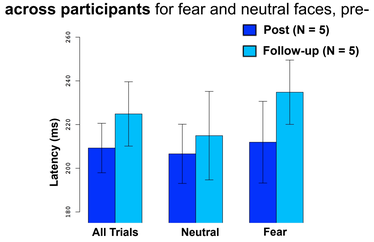

Figure 5: RN170 latency in the subset of children who completed a follow-up assessment (N = 5)

Figure 6: LN170 amplitude in waitlist controls (N = 3)

Conclusions

- A 16-week course of PRT for young children with ASD resulted in improved efficiency of neural indicators of social perception (RN170 latency), as well as a less atypical lateralization of the face-sensitive N170 response. These findings suggest focal treatment effects on social brain processes
- A decrease in the latency of a low-level sensory ERP component (P1) to neutral faces was observed post-treatment, suggesting that PRT caused a more rapid orienting of processing resources to neutral face stimuli
- No significant effects on P3 amplitude were observed, perhaps due to large inter-subject variability of the component's amplitude and shape over the chosen latencies
- Follow-up data showed no significant changes in P1 latency, LN170 amplitude, or RN170 latency between the end of treatment and a 16-week follow-up evaluation, supporting the hypothesis that the effects of treatment persist beyond the duration of the intervention
  - RN170 latency at follow-up showed a marginally significant increase from post-treatment, indicating that ongoing treatment may be necessary to maintain this effect
    - Further study is warranted to relate post-treatment brain responses to loss of behavioral gains from treatment
- The preliminary waitlist control results show values trending in the opposite direction of those of the children receiving the intervention, suggesting that observed changes are not simply a function of development
  - Several effects in the waitlist and follow-up subgroups showed trends toward significance, highlighting the need for larger samples to confirm these findings
- These findings provide the first evidence of improved neural efficiency resulting from PRT
  - In concert with fMRI results following a 16-week course of PRT, these ERP findings inform understanding of brain mechanisms underpinning positive response to behavioral treatment

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