Visual Preferences in Infants at High-Risk for Autism: Behavioral and Psychophysiological Cross-Group Comparisons

Bridgette Tonnsen, M.A., Nicole Zieber, Ph.D., Jane Roberts, Ph.D. , John Richards, Ph.D.
University of South Carolina

INTRODUCTION

Recent estimates suggest **1 in 54** males are diagnosed with an autism spectrum disorder (ASD), indicating a critical public health concern (CDC, 2012).

Some studies of infant siblings of children with autism (ASIBs) suggests atypical responses to faces (e.g. McCleery et al., 2009) and atypical patterns of face versus object preferences (e.g. Bhat et al., 2010) compared to typically developing (TD) controls. Others have reported similar fixations toward familiar and unfamiliar faces but atypical patterns of event related potentials (ERPs) across groups (Elsabbagh et al., 2009; Key & Stone, 2012). **However, no published studies have compared visual processing in ASIBs to other groups at high genetic risk for autism, including infants with fragile X syndrome (FXS), the leading known heritable cause of autism.**

Infant siblings of children with autism (ASIBS) comprise the most commonly studied high-risk prospective sample, as ASIBS face higher rates of autism diagnoses (10-61%; e.g. Landa & Garrett-Mayer, 2006) than the general population (1-2%).

Between 25% and 60% of **infants with fragile X syndrome (FXS)** later meet criteria for autism, and up to 90% display autistic symptoms. Fragile X syndrome is the most common heritable form of intellectual disability **and the leading single-gene cause of autism**, affecting 1:4000 individuals (Crawford et al., 2002).

RESEARCH QUESTIONS

Do high and low-risk infants differ in responses to novel faces and toys, as measured by:
(a) Behavioral looking preference toward novel stimuli
(b) Stimulus-onset ERPs implicated in novelty (Nc)

PARTICIPANTS

Preliminary data include participants from an ongoing longitudinal study of the emergence of autism in high risk infants.

	n	*n* male	Age in months (SD)
FXS	11	8	12.35 (.42)
ASIB	11	10	13.06 (.97)
Controls (TD)	8	6	12.55 (.29)
TOTAL	30	24	12.67 (.70)

Funded by NICHD-R37 18942 (Richards), NIMH-R01 090194 (Roberts), and NIMH-F31 095318 (Tonnsen).

METHODS:

A Paired Comparison task was used to examine visual preferences toward familiar and unfamiliar faces and toys. Four stimuli were presented: the child's mother and favorite toy, and the previous participant's mother and favorite toy. Infants viewed paired comparison trials of simultaneously-presented faces (mother, stranger) or toys (familiar, unfamiliar). **Preference scores** were calculated as the proportion of time looking toward the unfamiliar stimulus.

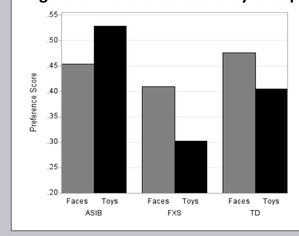
Infants also viewed brief presentations (500ms) of each stimulus for the purpose of measuring ERPs implicated in novelty (Nc). Event related potentials were recorded using a 128-channel high-density net.

The **Nc** in a negatively polarized component over frontal and central electrodes (peak latency 400-800ms). This component is associated with orienting attention and is generally larger to novel stimuli than familiar stimuli. Relevant to the present study, younger infants (<12-24m) have been reported to show greater Nc amplitude toward mother versus stranger faces, whereas older infants show larger Nc toward a stranger versus their mother, perhaps reflecting a shift from attachment-related maternal focus to interest in new social stimuli (e.g. Burden et al., 2007).

RESULTS: Behavioral Preferences

Behavioral data were analyzed using repeated measure analyses of variance (Figure 1). Patterns of novelty preference differed across stimuli and groups, $F(59, 733)=6.97$, $p<.001$. Although the FXS and TD groups showed greater novelty preference on face trials than toy trials, the ASIB group showed opposite patterns, demonstrating greater novelty preference on toy trials than face trials.

Figure 1: Preference Scores by Group



Within face trials, stranger preference marginally differed by group ($p=.07$), with the FXS group showing less stranger preference than the TD group. Preference toward unfamiliar toys also differed by group ($p<.001$), with the ASIB group showing the greatest novelty preference, followed by the TD and FXS groups.

Thus, although the FXS group exhibited less novelty preference overall, they followed the typical pattern of greater preference toward novel faces than toys. The ASIB group exhibited similar overall novelty preference to the TD group but exhibited atypically greater preferences toward novel toys versus faces.

RESULTS: Event-Related Potentials

Figure 2: FzCz Nc Response by Group

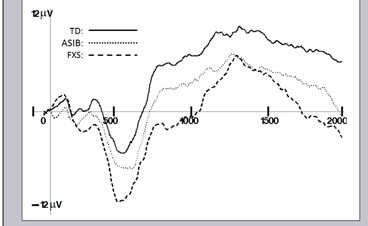
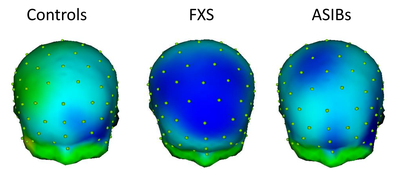


Figure 3: Nc Scalp Topography Plots Across Groups



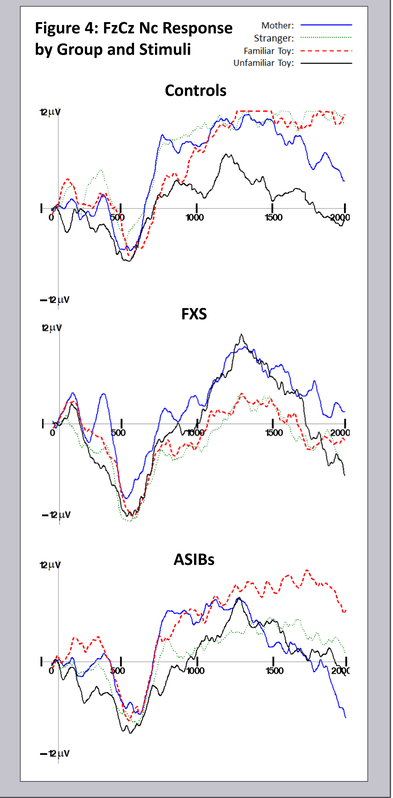
Data averaged over 450-750 ms at +/- 12 mV

Visual inspection of ERP grand averages suggests atypical Nc patterns in both high risk groups. Both FXS and ASIB groups produced larger Nc components than controls, with the greatest amplitudes in the FXS group (Figure 2).

Within toy trials, TD and ASIB participants showed greater Nc amplitude toward familiar versus unfamiliar toys, whereas the FXS group showed similar amplitudes across stimuli (Figure 4). Face trials also differed by group. Although the TD group produced a slightly greater Nc amplitude toward the stranger versus mother, the FXS group exhibited greater responses toward mothers versus strangers, and the ASIB group showed similar amplitudes across stimuli. The peak of the Nc also occurred later in response to faces in ASIBs, whereas peaks occurred later in response to objects for FXS and TD groups.

These data may suggest a developmental lag in shifting preferential attention toward strangers versus mothers in ASIBs and FXS, as well as atypical Nc latency associated with processing faces in ASIBs.

Figure 4: FzCz Nc Response by Group and Stimuli



DISCUSSION

Atypical face processing is well-documented in autism and may relate to the socio-communicative deficits inherent to the disorder. Our data suggest:

- **Infants with FXS** show **lower overall novelty preference** and fail to show greater Nc amplitude to familiar vs. unfamiliar toys. However, they show **typical face-specific novelty preferences** and typically shorter Nc latency to faces than toys.
- **Infant ASIBs** show **typical overall novelty preference** and Nc amplitude differences across familiar and unfamiliar toys. However, they show **comparatively less novelty preference for faces**, as well as longer Nc latency to faces.
- Diverging novelty preference patterns across high-risk groups underscore the importance of **cross-group comparisons** to inform the latent heterogeneity of autism
- Characterizing early visual preferences may contribute to **early detection and intervention** of efforts. For example, Nc latency to a mother's face is associated with stronger interpersonal skills in ASIBs (Key & Stone, 2012), suggesting face-specific early indicators may be linked to clinical outcomes.
- Future work is needed to test the **generalizability of early autism indicators** from ASIB samples, as well as the clinical implications of markers shared across high risk groups

REFERENCES

Bhat, A.N., Galloway, J.C., & Landa, R.J. (2010). Social and nonsociala visual attention patterns and associative learning in infants at risk for autism. *Journal of Child Psychology and Psychiatry, 51*, 989-97.
Burden, M. J., Westurlund, A. J., Armony-Sivan, R., Nelson, C. A., Jacobson, S. W., Lozoff, B. ... Jacobson, J. L. (2007). An event-related potential study of attention and recognition memory in infants with iron-deficiency anemia. Pediatrics, 120, e336-45.
Center for Disease Control and Prevention. (2012). Prevalence of autism spectrum disorders - Autism and developmental disabilities monitoring network. *Surveillance Summaries, 61(SS03),* 1-19.
Crawford, D.C., Acuna, J. M., & Sherman, S. L. (2001). FMR1 and the fragile X syndrome: human genome epidemeology review. *Genetic Medicine, 3*, 359-71.
Elsabbagh, M., Volein, A., Csibra, G., Holmboe, K., Garwood, H., Tucker, L. ... & Johnson, M.H. (2009). Neural correlates of eye gaze processing in the infant braoder autism phenotype. *Biological Psychiatry, 65*, 31-8.
Key, A. P. & Stone, W. L. (2012). Processing of novel and familiar faces in infants at agerage and high risk for autism. *Developmental Cognitive Neuroscience, 2,* 244-55.
Landa, R. & Garrett-Mayer, E. (2006). Development of infants with autism spectrum disorders: A prospective study. *Journal of Child Psychology and Psychiatry, 47,* 629-38.
McCleery, J.P., Akshomoff, N., Dobkins, K. R., & Carver, L. J. (2009). Atypical face versus object processing and hemispheric asymmetries in 10-monthold infants at risk for autism. *Biological Psychiatry, 66,* 950-7.