RECRUITMENT OF A PARTIALLY OVERLAPPING NETWORK DURING IMPLICIT LEARNING IN ASD AND TYPICAL DEVELOPMENT

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INTRODUCTION

- Symptoms of Autism Spectrum Disorders (ASD) suggest impairment in social, language and motor skills (APA, 2000).
- In typically developing children, the acquisition of such skills is supported by implicit learning (Pacton & Perruchet, 2006).
- We have previously demonstrated that implicit sequence learning is intact in children with high-functioning ASD (Barnes et al., in press, but see Mostofsky et al., 2000).
- In typically developing adults, implicit sequence learning is known to depend upon dynamic changes in frontal, striatal, and cerebellar activation (Doyon & Benali, 2005). However, little is known about the neural basis of implicit sequence learning in childhood ASD.

QUESTION

- How do neural changes during the timecourse of probabilistic sequence learning differ between children with ASD and matched controls?

METHOD

Participants

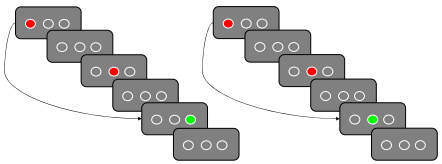
Group	Sample Size (# male)	Age (SD)	Full Scale IQ (SD)
ASD	13 (11)	9.48 (1.66)	120.2 (19.8)
CON	13 (10)	9.98 (1.17)	121.5 (14.4)

- ASD diagnosis confirmed by clinician using ADI and ADOS
- Groups were matched for gender, age, and Full Scale IQ (*p*s > .38)
- Children with ASD were unmedicated at the time of the study

TASK PARAMETERS

High Probability Trial (80% of Trials)

Low Probability Trial (20% of Trials)

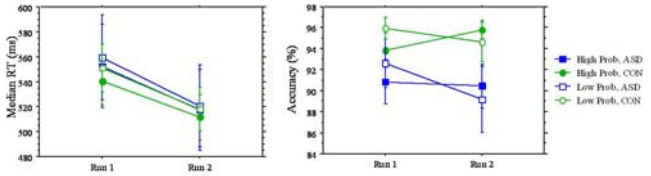


- Participants completed two runs lasting 6:20 min and comprising 135 trials each
- Event-related design; stimuli presented in fixed, pseudorandom order using OptSeq2
- Each trial comprised a three-event sequences [2 cues (red circles) and 1 target (green circles)]
- Participants instructed to respond to target location with Right Hand
- Unbeknownst to participants, location of the 1st Cue location probabilistically predicted location of the Target
  - High Probability Trials
  - Low Probability Trials
- Cue and Target location counterbalanced
- Performance speed and accuracy examined in a Group x Run x Probability repeated measures ANOVA

fMRI PARAMETERS AND ANALYSIS

- Siemens 3T Trio magnet, T2* sensitive gradient EPI acquisition
- 152 images/run, 42 axial slices, 3.7 mm thick; TR 2500 ms, TE 30 ms, 90˚ flip angle, FOV = 256 x 256, 4 mm inplane resolution
- Data analysis in SPM5: Slice-time correction, motion correction, spatial normalization, spatial smoothing (8 mm FWHM gaussian); Region of Interest (ROI) analysis in MARSBAR
- First, to determine regions showing learning-related changes, linear, parametric changes in activation over time related to task (i.e., all correct High Probability and Low Probability trials; henceforth, $TASK_{\Delta t}$) and baseline (henceforth, $Null_{\Delta t}$) were computed for each subject.
- Second, to examine regions differing by group, a Group (ASD vs. CON) x Condition ($Task_{\Delta t}$ vs. $Null_{\Delta t}$) ANOVA was computed.
- Third, significant clusters from the Group x Condition interaction were identified as ROIs, yielding 11 ROIs [from Anterior to Posterior: SFG (BA 8); IFG (BA 47); MFG (BA 6); SFG (BA 6); ACC (BA 24); MTG (BA 21); CC (BA 24); MTG (BA 21); SPC (BA 7); IOG (BA 18); Cerebellum].
- Fourth, a Group (ASD vs. CON) x Probability (High Probability vs. Low Probability) ANOVA was computed to test for Group x Probability interactions in each ROI.
- Thresholds: Group x Condition ANOVA: $p < .005$, uncorrected, k = 10; ROI Analysis: $p < .05$, uncorrected

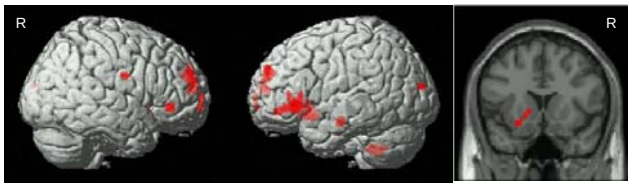
BEHAVIORAL RESULTS



- Overall performance did not differ by group (RT, $p = .86$, Accuracy, $p = .11$).
- Performance was faster across runs (RT, $p < .0001$, Accuracy, $p = .38$).
- Performance was marginally faster on High Probability than Low Probability trials ($p = .08$; Accuracy, $p = .22$).
- Learning did not differ by group (Group x Probability interaction: RT, $p = .66$; Accuracy, $p = .88$).

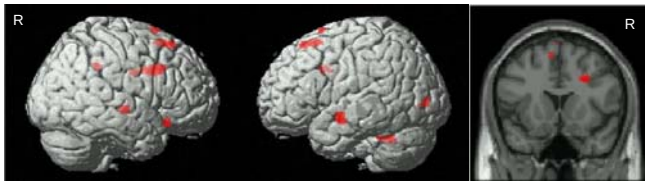
fMRI RESULTS

A prefrontal-striatal-cerebellar network showed linear changes in activation during the task relative to baseline (Main Effect of Condition).



(y = -16)

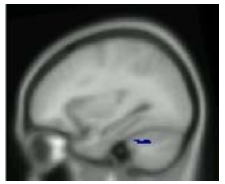
A premotor-cerebellar network showed group differences in linear changes in activation during the task relative to baseline (Group x Condition interaction).



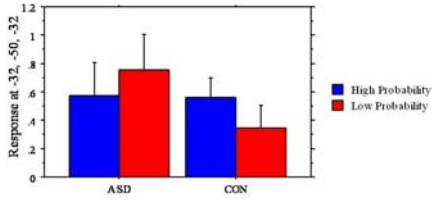
(y = -16)

ROI RESULTS

Only one ROI (of 11) in the left cerebellum near Lobule VI was sensitive to group differences in the response to probability (Group x Probability interaction, $p = .04$).



(x = -32)



SUMMARY

- Overall, learning was associated with changes in activation of a prefrontal-striatal-cerebellar network.
  - This is consistent with studies examining the neural basis of implicit sequence learning in typically developing children and adults.
- Groups differed in activation of a premotor-cerebellar network during learning.
  - This is consistent with functional neuroimaging studies in adolescents and adults with ASD (Müller et al., 2004) and extends them to a novel probabilistic sequence learning paradigm.
- Cerebellar activation was greater for novel sequences in children with ASD, whereas activation was greater for familiar sequences in control children.
  - Cerebellar sensitivity to probabilistic information is qualitatively different in children with ASD and control children.

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Funding by Autism Speaks (NAAR), The Frederick & Elizabeth Singer Foundation, Georgetown University, and NIH