Neuropsychological correlates of thalamocortical connectivity in Autism Spectrum Disorders (ASD)

Aarti Nair1,2, Merage Ghane1, Amanda J. Khan1, Jose O. Maximo1, Ralf Schuster3, Ralph Axel-Müller1,2
1. Brain Development Imaging Lab, Department of Psychology, San Diego State University, San Diego, CA 92120
2. Joint Doctoral Program in Clinical Psychology, San Diego State University & University of California, San Diego, CA 92120

Background

- Thalamus is an important subcortical relay structure, through which almost all sensory information is routed.
- It plays a crucial role in visual, auditory, and somatosensory functions, as well as attention and motor control.
- Highly specific patterns of thalamocortical connectivity have been demonstrated in typically developing individuals (TD) using functional magnetic resonance imaging (fMRI; Zhang et al., 2008; 2010; Fair et al., 2010).
- Autism spectrum disorders (ASD) are characterized by deficits in social interaction and communication, along with repetitive or restrictive patterns of behaviors of interests (DSM-5, 2000).
- Various lines of evidence have suggested thalamic abnormalities in ASD (e.g., Chugani et al., 1997; Friedman et al., 2003). However, little is known about the integrity of thalamocortical connectivity in ASD.

Objective

Objective of present study was to assess patterns of thalamocortical connectivity in adolescents with ASD, compared to a TD control group, and to assess if connectivity strength was related to scores on relevant neuropsychological and diagnostic measures.

Results

- Compared to the TD group, ASD participants mostly showed a pattern of thalamocortical underconnectivity for the prefrontal, parietal, motor and somatosensory ROIs, whereas connectivity between temporal ROIs and thalamus was greater in the ASD than the TD group, especially in the right hemisphere.
- Right hemisphere tempo-thalamic connectivity was positively correlated with the Social Motivation (r = .31, p < .05) and Autistic Maneriisms (r = .36, p = .02) subdomains on the SRS. This indicates that right hemispheric tempo-thalamic overconnectivity in ASD may be associated with impaired social interaction and stereotypical behaviors.
- Additional, negative correlations were seen for motor network connectivity in the right hemisphere with AODS communication scores (r = -.39, p < .01) and the ADI social interaction index (r = -.36, p = .03). This suggests that motor-thalamocortical underconnectivity observed in ASD group may be associated with deficits in social communication and social interaction skills.
- For the left hemisphere, negative correlations were seen between parietal-occipital thalamocortical connectivity and the Metacognition index of the BRIEF (r = -.56, p = .01), indicating that left parietal-occipital thalamic underconnectivity in ASD group may be associated with deficits in metacognitive skills (organizing thoughts, problem solving, working memory).

Methods

Data acquisition:
- fMRI - GE 3T Aria750 scanner with 8-channel head coil. FSPGR T1-weighted anatomical sequence (180 slices, 1mm thickness). 6-minute resting-state functional EPI (180 whole-brain volumes, TR: 2000ms; TE: 30ms; 3.4mm slice thickness; in-plane resolution 3.4mm).
- Neurophysiological & Diagnostics - Weecher Abbreviated Intelligence Scale (WAIS), Developmental Test of Visual-Motor Integration (VMI), Autism Diagnostic Interview - Revised (ADI-R), Autism Diagnostic Observation Schedule (ADOS), Social Communication Questionnaire (SCQ), Social Responsiveness Scale (SRS), and Behavior Rating Inventory of Executive Function (BRIEF) - parent version.

Participants:

<table>
<thead>
<tr>
<th></th>
<th>TD (n=21)</th>
<th>ASD (n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 left hand; 1 female</td>
<td>1 left hand; 1 female</td>
</tr>
<tr>
<td>Mean Range SD</td>
<td>Mean Range SD</td>
<td>p</td>
</tr>
<tr>
<td>Age</td>
<td>14.4 12.1-16.8 1.5</td>
<td>14.9 12.1-17.1 1.5</td>
</tr>
<tr>
<td>IQ</td>
<td>109 88-126 10.7</td>
<td>114 87-141 14.1</td>
</tr>
</tbody>
</table>

Regions of Interest:

- Cortical ROIs based on Zhang et al. (2008): prefrontal, motor, somatosensory, temporal, and parietal-occipital cortex (see Fig. 1 for details).
- Thalamus masks obtained from AFNI Talairach-Tournoux atlas.

Data Processing and Analyses:
- FcMRI preprocessing done using AFNI.
- Six rigid-body motion parameters and physiological measures (cardiac, respiratory) modeled as nuisance variables and removed with regression.
- Partial correlation maps obtained for connectivity between cortical ROIs and thalamus, i.e., for each ROI-thalamic network partial correlation maps obtained while controlling for the effect of the connectivity between the other four ROIs and the thalamus.
- Mean Z7 obtained for each cortical seed for all participants for Pearson’s correlation analyses with scores on neuropsychological measures.

Conclusion

- FcMRI findings suggest partially reduced functional connectivity between thalamus and frontal, parietal-occipital, and motor cortices. This is consistent with previous studies suggesting compromised thalamocortical connectivity in ASD (e.g., Chugani DC, Muzik O, Rothermel R, et al. Altered serotonin synthesis in the dentatothalamocortical pathway in autistic boys. J Neurophysiol. 2002;88:224-232).
- Tempo-thalamic connections were found to be atypically enhanced (especially in the right hemisphere). This is consistent with literature suggesting anatomical (e.g., Hardin et al. 2006; Lee et al. 2007) and functional (e.g., Castelli et al. 2002, Boddaert et al., 2003) abnormalities in the temporal lobe ASD.
- Underconnectivity observed in the motor-thalamic network and overconnectivity in the right tempo-thalamic network may be associated with deficits in social communication and social interaction, which represent core diagnostic criteria for ASD. Atypical connectivity patterns in these networks therefore appear to be associated with autistic symptomatology.
- Results also suggest that stereotyped autistic behaviors (e.g., unusual sensory interests, repetitive speech, repetitive or odd motor behaviors) may be associated with overconnectivity in the right tempo-thalamic network. However, current analyses could not identify which specific regions within the temporal lobe showed such overconnectivity with thalamus.
- Executive deficits—specifically metacognitive skills such as problem solving, initiating activity, organizational abilities—appears to present with reduced thalamocortical connectivity of parietal-occipital regions.

References

- Boddaert et al. 2002, Boddaert et al., 2003 abnormalities in the temporal lobe ASD.
- Castelli et al. 2002, Boddaert et al., 2003 abnormalities in the temporal lobe ASD.
- Friedman et al. 2003).