

## Thalamo-cortical functional connectivity in Autism Spectrum Disorders

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### Introduction

Autism Spectrum Disorders (ASD) are prevalent developmental disorders characterized by deficits across multiple functional domains, including motor, sensory, behavioral, and cognitive functions. Whereas the mechanisms underlying ASD are not known, there is increased evidence that abnormal brain development and impaired brain connectivity are associated with the disorder (1). Thalamus is one of the major brain structures that has an essential role in brain development and connectivity and is involved in many cognitive processes. Several studies have indicated both structural and functional abnormalities of the thalamus in autism (2-4). Increased thalamo-cortical connectivity was observed in autism versus a control group during a visuomotor coordination task (4). In this study, we examine the functional connectivity of the thalamus with the prefrontal, motor, somatosensory, parieto-occipital, and temporal cortices during rest in a group of young adults with ASD versus a typically developing control group.

### Methods

Functional, field map and anatomical data were obtained for 14 participants with a diagnosis of high functioning autism disorder (ASD) and 15 typically developing (TD) individuals with ages between 18 and 25 year old using a 3T Siemens scanner. Diagnosis was confirmed using ADOS for all ASD participants and ADI-R for 10 subjects for who a caregiver was available to participate. IQ measures were obtained for all participants using WAIS-III. There were no significant differences between the two groups on age (TD:  $21.8 \pm 2.0$ , ASD:  $21.7 \pm 2.3$ ,  $p=.85$ ) and full scale IQ (TD:  $111 \pm 11$ , ASD:  $109 \pm 17$ ,  $p=.766$ ). Bold functional images were obtained using T2\*-weighted EPI with TR=2000ms, TE=29ms, flip angle=90°, 36 slices, and a voxel size of  $3.12 \times 3.12 \times 3.2 \text{ mm}^3$ . Resting-state data was acquired for 6 min 40 s. Participants were required to relax with their eyes closed and refrain from moving and falling asleep.

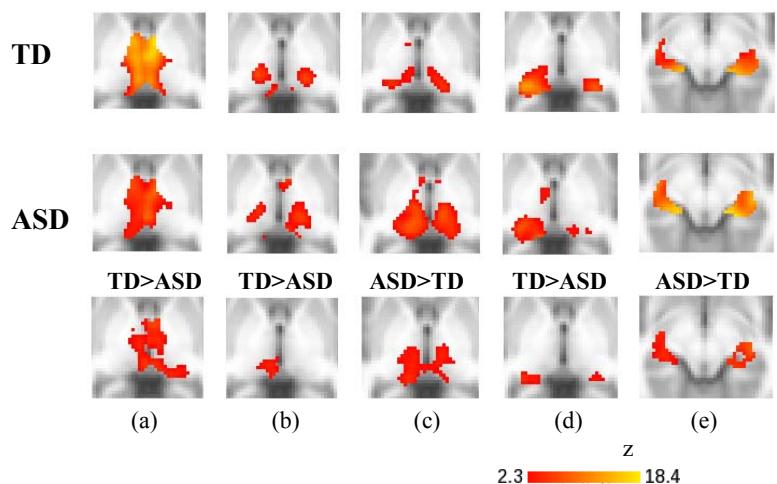
**Image processing:** Functional MRI data was processed similar to Fair et al. (5) using AFNI and FSL software packages. The preprocessing steps included correction of image distortions due to B0 field inhomogeneities using the acquired field map, slice timing and motion correction, smoothing using a 6mm FWHM Gaussian kernel, linear trend removal, temporal bandpass filtering ( $0.009 \text{ Hz} < f < 0.08 \text{ Hz}$ ), regression of the six motion parameters and of the white matter and cerebrospinal fluid signal. Prefrontal, motor, somatosensory, parieto-occipital, and temporal cortical regions were segmented for the right and left hemisphere for each subject using an automated procedure. Average resting state timeseries were obtained for all the cortical regions of interest. A partial correlation procedure was employed to find the thalamic voxels that correlate with cortical timeseries in each subject (5). Analyses were performed separately for the two hemispheres. Higher level analyses were carried out using a fixed effects model in FEAT, part of FSL. Z statistic images were thresholded using clusters determined by  $Z > 2.3$  and a corrected cluster significance threshold of  $p=0.05$ .

### Results

Functional connectivity of the thalamus with all the cortical regions was observed for both groups (Figure 1). Increased prefrontal and parieto-occipital thalamic connectivity were observed in the control versus the autism group for both right and left hemispheres (Figures 1a and 1d). Increased thalamo-motor connectivity was also observed in the control group for the right hemisphere only (Figure 1b). The autism group presented increased thalamo-somatosensory (Figure 1c) connectivity compared to the control group. Increased temporal lobe connectivity with the medial geniculate nucleus thalamic region was also observed in the ASD versus TD group (Figure 1e).

### Discussion

The results presented here support the hypothesis of atypical thalamo-cortical connectivity in young adults with ASD. Thalamo-cortical connectivity in typical developing brain undergoes a maturation process that involves strengthening of the prefrontal connectivity and reduction of the temporal thalamic connectivity with age (5). The results presented here may be due to a slower shift of the thalamic connectivity to the prefrontal regions and are consistent with the protracted and atypical brain development in autism that is usually seen in later childhood and adolescence (6). One limitation of this study is the relatively small number of participants. Findings need to be confirmed in larger populations.



**Figure 1.** Functional connectivity patterns of the (a) prefrontal, (b) motor, (c) somatosensory, (d) parieto-occipital, and (e) temporal cortices with the thalamus.

Top row: Control group; Middle row: ASD group; Bottom row: Group differences, with the group showing the stronger connectivity indicated for each region.

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