Reliability of reduced inter-subject functional connectivity during naturalistic movie-watching fMRI in autism - comparison of German and Finnish samples

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Introduction

Autism is a neurodevelopmental disorder, which may also be associated with altered sensory responsivity to external stimuli. Naturalistic functional magnetic resonance imaging (fMRI) is a useful way to characterize brain activity in real-life stimuli (e.g. movie-watching). Inter-subject functional connectivity (ISFC) is sensitive to stimuli-driven neural coupling across individuals and appears to characterize the potential idiosyncrasy of brain activity in the group of autistic participants (Bolton et al., 2018). The aim of our study is to investigate idiosyncrasy by examining ISFCs between adults with autism (AUT) and neurotypical (NT) individuals and to validate potential findings using cross-country datasets (German and Finnish samples).

Methods

German dataset, visual-only: N_{NT} = 25, N_{AUT} = 22; Finnish dataset, audiovisual,: N_{NT} = 19, N_{AUT} = 18. Several short clips of Hollywood movies depicting social-emotional scenes (i.e., emotion, neutral, social interaction, non-interaction, pain) were played to participants during 3T fMRI scanning (TR Germany=2s, Finland=2.6s). The detailed steps of method are illustrated below in Figure 1.

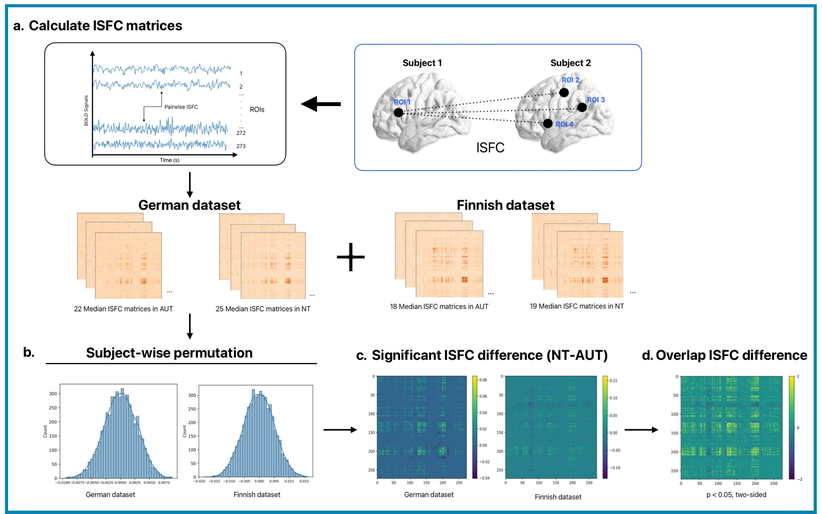

Figure 1. Methods in steps. a. ISFC matrices were calculated for four participant group: German/Finnish AUT/NT group using Brainnetome (Fan et al., 2016) and cerebellum atlas (Diedrichsen et al., 2009, 2011) with 273 ROIs. Median pairwise ISFC values were obtained for each participant group; b. Subject-wise permutations were conducted 5000 times for the difference of ISFC (NT-AUT) in German and Finnish dataset; c. The significant ISFC differences in two datasets were calculated based on the permutated distributions, at p < .05 and p < .01 (two-sided); d. The overlap ISFC difference across two datasets were computed as the intersection of two matrices in step c. The replication rate of ISFC difference in German and Finnish datasets were calculated at p < .05 (two-sided).

Results

- The peak ISFCs were lower in AUTs than NTs in similar brain regions in two datasets (Figure 2a), with overall lower ISFC group difference in the German than in the Finnish dataset (Figure 2b).
- Both datasets showed lower ISFCs between visual (e.g., occipital gyrus, cuneus) and parietal regions (e.g., superior/inferior parietal lobules) in AUT compared to NT individuals. The overall regions were similar (Figure 3). For overlap of ISFC group differences in two datasets, see Figure 4-5.

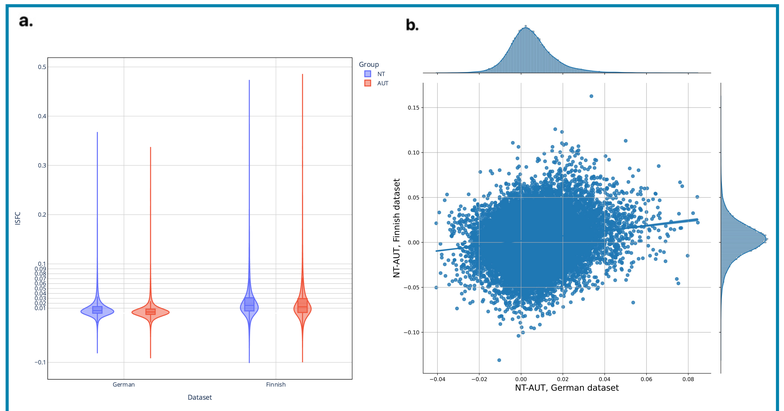

Figure 2. ISFC distribution across AUT and NT groups in two datasets. a. Violin plots of pairwise median ISFC values. For each group (purple for NT, red for AUT) and each dataset (left for German, right for Finnish). The horizontal line within each violin plot represent the median ISFC value for that specific group; b. Scatterplot of ISFC difference in two datasets, with German dataset on the x-axis and Finnish dataset on the y-axis. The distributions of the ISFC differences are shown at the top (for German dataset) and on the right (for Finnish dataset).

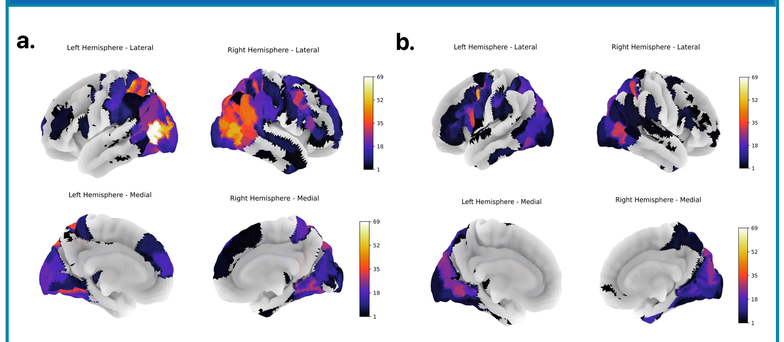

Figure 3. Count maps of ROI regions with significant ISFC group difference (NT–AUT), p < .01. a. Count in German dataset; b. Count in Finnish dataset. The maximum count of significant ROIs is 69 for the German dataset and 48 for the Finnish dataset. Only positive ISFC difference values were counted and visualized here.

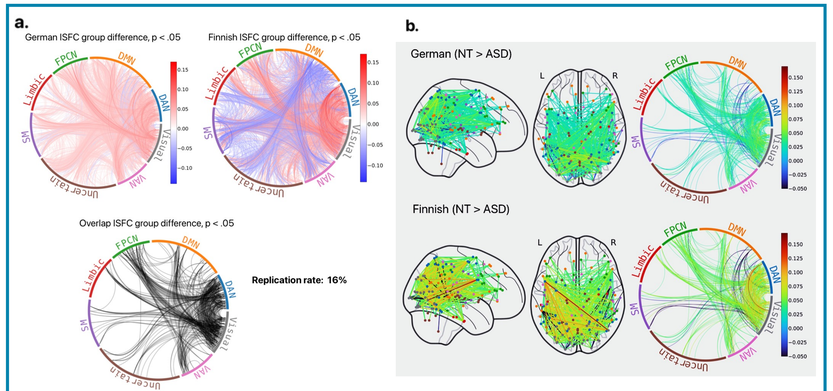

Figure 4. Connectome maps in two datasets and their overlap. a. Significant ISFC group differences (NT-AUT) in two datasets (German, top left; Finnish, top right) and their ROI-to-ROI overlap results (bottom, without numerical values). b. Overlap ISFC group differences with values, p < .05. Both positive and negative ISFC difference values were visualized. DMN, Default mode network; DAN, Dorsal attention network; VAN, Ventral attention network; SM, Somatomotor network; FPCN, Frontparietal control network; Uncertain, Subcortical regions.

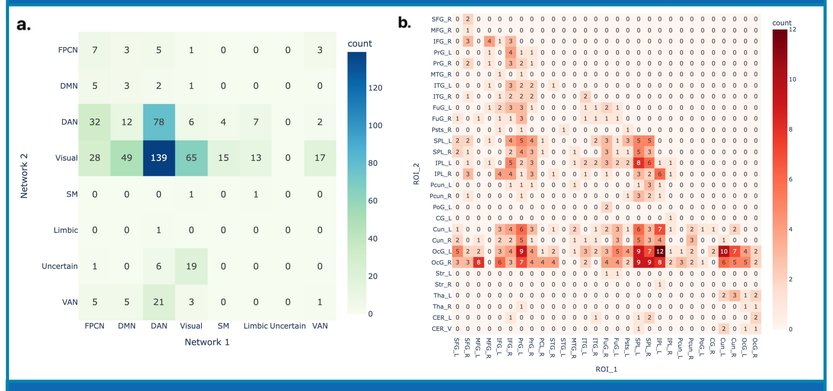

Figure 5. Count heatmaps of significant overlap ISFC group differences mapped in two atlas. a. With Yeo 7-network atlas. Visual network showed the greatest ISFC difference with other networks (sorted: DAN, DMN, FPCN, VAN, SM, Limbic); b. With Brainnetome & Cerebellum atlas. SFG, Superior Frontal Gyrus; MFG, Middle Frontal Gyrus; IFG, Inferior Frontal Gyrus; PrG, Precentral Gyrus; PCL, Paracentral Lobule; STG, Superior Temporal Gyrus; MTG, Middle Temporal Gyrus; ITG, Inferior Temporal Gyrus; FuG, Fusiform Gyrus; Psts, Posterior Superior Temporal Sulcus; SPL, Superior Parietal Lobule; IPL, Inferior Parietal Lobule; Pcun, Precuneus; PoG, Postcentral Gyrus; CG, Cingulate Gyrus; Cun, Cuneus; OcG, Occipital Gyrus; Str, Striatum; Tha, Thalamus; CER, Cerebellum; L, left hemisphere; R, right hemisphere; V, vermis.

Discussion

- Overlapping ISFC differences clustered between visual (e.g., OcG) and parietal regions (e.g., left IPL, SPL) across both datasets (Figure 5b). These differences might be related to abnormal process of social cognition (Igelström & Graziano, 2017). SPL supports visual searching (Bueichekú et al., 2015). Weaker ISFCs between SPL and visual regions might suggest less searching towards visual targets during movie-watching among AUTs.
- The absence of a soundtrack in the German dataset might contributed to cross-dataset differences in ISFC levels, and regions related to sound and speech (e.g., STG/MTG).
- The current findings confirmed the reliability of reduced ISFCs during naturalistic movie-watching fMRI in adults with autism compared to neurotypicals, although only a subset of group differences was replicated across the German and Finnish datasets.

References

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