Sex-Linked White Matter Microstructure of the Social and the Analytic Brain

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Introduction

At a population level, a great number of compelling evidence suggested that sexual dimorphism in the brain can underpin sex differences in both cognitive and neuropsychological behaviors. According to the empathizing-systemizing (E-S) theory posited by Simon Baron-Cohen, females were stronger empathizers while males were stronger systemizers [1]. Empathizing, driven by the social brain, refers to the capacity to predict and to respond to the behavior of agents by inferring their mental status and to respond to these with an appropriate emotion. Systemizing, based on the analytic brain, is the capacity to predict and to respond to the behavior of non-agentive deterministic systems by analyzing input-operation-output relations and inferring the rules that govern such system [2]. However, for all we know, the white matter (WM) microstructure associated with the social and analytic brain as indicated by sex differences remains to be investigated. Here, we applied the Tract-Based Spatial Statistics (TBSS) [3] on diffusion tensor image, concurrently with the assessments of Empathizing Quotient (EQ) [4] and Systemizing Quotient (SQ) [5], for the healthy female and male adults, to investigate the sex-linked white matter microstructure in aspects of the social brain and the analytic brain.

Methods

Eighty healthy right-handed participants (40 Female / 40 Male) were enrolled in the study. The female and male subgroups were matched in age [25.5±7.2 y/o vs. 25.2±6.4 y/o] and education years [15.0±2.7 years vs. 15.2±2.2 years]. All MR scans were performed on a 1.5T MR system (Excite II; GE Medical Systems, Milwaukee, Wis., USA) at the Veterans General Hospital Taipei. Whole brain diffusion-weighted images were acquired using single shot diffusion spin-echo EPI sequence with TR/TE = 17000/68.9 ms, voxel size = 2 x 2 x 2.2 mm^3, b = 900 s/mm^2, 13 directions, and NEX = 6. Whole brain voxel-wise statistic analysis of the FA map was carried out using TBSS approach, which was implemented in FSL (Oxford, UK). In order to investigate longitudinal (principal diffusion component, λ1) and radial (transverse diffusion component, [(λ2 + λ3)/2]) diffusivities at the same time, the non-linear warps and skeleton projection information obtained in TBSS procedure were also be applied to these two diffusivity maps. Voxel-wise statistical analysis of individual skeleton images of both groups for both contrasts (Female > Male) and (Female < Male), with age use as a covariate, was performed using a nonparametric permutation test with a cluster size threshold of T>3 and FWE corrected P<0.05 for significance. Prior to MRI scanning, all of the participants filled out a series of self-report dispositional measures including the EQ [4] and the SQ [5]. To further elucidated sex difference in the correlation between dispositional measures and regional FA value, we performed a voxel-by-voxel interaction analysis to test for areas showing linear interactions between group and dispositional measures. The statistic criteria of this interaction analysis were the same as described above.

Results

Dispositional Measurements:

The analysis of the dispositional measures revealed a major effect in the measure [EQ vs. SQ: $F_{1,78}$= 48.044, P< 0.001] as well as their interaction with group [$F_{1,78}$= 20.835, P< 0.001]. The effects were mainly driven from the double dissociation between sexes. Females scored higher on EQ whereas males scored superior on SQ.

Regional DTI Indices Difference Between Two Groups:

Direct group comparison showed that the male exhibited greater FA but reduced radial diffusivity in several clusters including the bilateral anterior limb of internal capsule, left superior longitudinal fasciculus, left inferior longitudinal fasciculus, bilateral inferior fronto-occipital fasciculus, bilateral uncinate fasciculus, left putamen, left middle frontal gyrus, bilateral medial frontal gyrus, bilateral fusiform gyrus, left superior temporal gyrus, anterior division of bilateral parahippocampal gyrus, left insula, left postcentral gyrus, bilateral precuneus, and the posterior lobe of right cerebellum (Fig1 A-I). Conversely, female exhibited greater FA in left inferior fronto-occipital fasciculus, the body of corpus callosum, posterior division of bilateral parahippocampal gyrus, and the anterior lobe of left cerebellum (Fig1 J-M). These regions with greater FA in females were associated with a decrease in radial diffusivity.

Interaction of Dispositional Measures by Sexes

The interaction analysis indicated that the regions with FA associated with dispositional measures of empathy reflected sex differences in the social cognition network (Fig2 A-B). Specifically, the FA value of the left inferior parietal lobule, superior temporal gyrus, and fusiform gyrus showed a positive correlation with the EQ in females whereas a negative correlation in males. In the contrast, the FA value of the left occipital cuneus, right precentral gyrus, and left middle frontal gyrus displayed a positive correlation with SQ in males but a negative correlation in females.

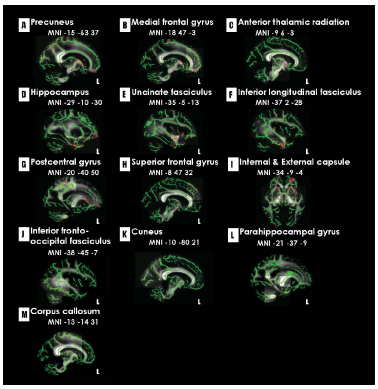

Figure 1.

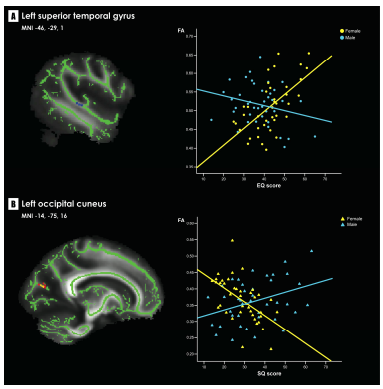

Figure 2.

Figure 1 : Sex differences in regional FA value

The regions showing significant sex-dimorphism were rendered onto the averaged FA map and its skeleton images of the whole sample. (Red: Male > Female ; Blue: Female > Male)

Figure 2 : Interaction of FA and dispositional measures between groups

A. Left superior temporal gyrus and Empathizing Quotient (EQ). B. Left occipital cuneus and Systemizing Quotient (SQ)

Conclusions

The present study demonstrated that sex differences of WM microstructures, as indicated by DTI index maps (FA, longitudinal and radial diffusivities), were associated with behavioral manifestations. The finding could not only offer insights to diseases with disturbed normal sexual dimorphism, e.g., schizophrenia or autism spectrum disorder but also provided evidence about imbalance long/short connection between female and male groups [1]. Specifically, the sexual dimorphisms of white matter microstructures can reflecte the social brain and analytic brain, which supported to the extreme male brain theory of autism, posited by Baron-Cohen [1].

Reference

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