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Research article

Relationship between white matter microstructure and work hours

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ABSTRACT

Human social activities are realized by a synergy of neuronal activity over various regions of the brain, which is supported by their connectivity. In the present study, we examined associations between social activities, represented by work hours, and brain connectivity as quantified using diffusion tensor imaging (DTI). In 483 healthy participants, DTI analysis was performed using 3 T magnetic resonance imaging, and work hours were calculated, considering hours of paid employment (the "Work for Pay" category), hours of housework (the "Work at Home" category), and hours of school-related study (the "Student" category). The correlations between each class of work time and DTI indices were analyzed. The mean diffusivity (MD) values of the anterior limb of the internal capsule (ALIC) and the superior fronto-occipital fasciculus (SFO) were negatively correlated with total work hours (ALIC: $r = -0.192$, $p = 2.3 \times 10^{-5}$; SFO: $r = -0.161$, $p = 3.8 \times 10^{-4}$). We also found that the MD values of the ALIC and the SFO were correlated with work hours in the Work for Pay category (ALIC: $r = -0.211$, $p = 3.2 \times 10^{-6}$; SFO: $r = -0.163$, $p = 3.4 \times 10^{-4}$) but not with those in the Work at Home category or the Student category. These results suggest that social activity is associated with the white matter microstructure of the ALIC and the SFO. The main difference between "Work for Pay" and the other two social activities appears to be the type of motivation—for example, external versus internal. Therefore, the white matter microstructure of the ALIC and SFO may be related to externally motivated social activities.

1. Introduction

The length of work hours is a measure that reflects how well a person is able to participate in a local or global human society. The Social Activity Assessment (SAA) which was developed by Sumiyoshi, et al. [32] based on the Modified Social Adjustment Scale–Work Outcome [30] and its Japanese version [33], is a useful scale for assessing three types of social activities [18,23,31]: paid employment (the Work for Pay category), housework (the Work at Home category), and school-related study for students (the Student category).

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There is a research finding that shows a potential relationship between social activities and brain structure. A previous imaging study demonstrated that superior frontal gyrus volume was positively correlated with domestic work hours and negatively correlated with paid work hours in women [36]. Because human social activities are realized by a synergy of neuronal activity over various regions of the brain, connectivity between brain regions may also be important. However, no study has been carried out to examine the relationship between human social activity and brain connectivity. Thus, our central question here is whether human social activities are associated with the characteristics of connectivity among brain regions.

Diffusion tensor imaging (DTI) is a powerful tool to reveal connectivity between brain regions. DTI visualizes the structure of cerebral white matter fibers and has been used in various brain connectivity studies [1]. In addition, indices quantified from DTI reflect the microstructure of cerebral white matter, such as the direction, diameter, density and thickness of myelinated axons in the white matter [12,16,27–29,34]. In the present study, we examined the correlation between social activities and three DTI indices—namely, fractional anisotropy (FA), mean diffusivity (MD), and radial diffusivity (RD)— that indicate different characteristics of brain connectivity.

2. Materials and methods

2.1. Participants

Four hundred and eighty-three healthy volunteers were enrolled in this study. Some of the participants' data have been included in our previous studies [6,7,14,15,19,20,22,24,37]. The demographic characteristics of the participants are summarized in Table 1. The participants were recruited from the community through local advertisements at Osaka University. The participants were excluded if they had current or past contact with psychiatric services; neurological disease; or medical conditions that could potentially affect the central nervous system, such as atypical headaches, head trauma with loss of consciousness, chronic lung disease, kidney disease, chronic hepatic disease, thyroid disease, active cancer, cerebrovascular disease, epilepsy, seizures, substance-related disorders, or intellectual disability. All participants provided written informed consent. All procedures were conducted according to the Declaration of Helsinki and approved by the ethical committee of Osaka University and the National Center of Neurology and Psychiatry.

2.2. MRI acquisition and DTI

DTI was acquired with two magnetic resonance imaging (MRI) scanners in accordance with our previous protocol as described below (Osaka1 and 2) [13]. In the Osaka 1 group, which contained 152 healthy volunteers, whole-brain axial DTI scanning was performed on a 3.0 T GE Signa HDxt scanner (GE Healthcare, Milwaukee, WI) using an eight-channel head coil with the following parameters: two-dimensional diffusion-weighted spin-echo echo planar imaging (EPI), repetition time (TR) = 15 s, echo time (TE) =82.9 ms, acquisition matrix = 96 × 96, reconstruction matrix = 256 × 256, array spatial sensitivity encoding technique (ASSET) acceleration factor = 2, field of view (FOV) = 260 × 260 mm, slice thickness = 3 mm, voxel size = 1.015 × 1.015 × 3 mm, number of slices = 48. A diffusion sensitization gradient was applied with 15 noncollinear gradient directions and a b value of 1000s/mm^2, in addition to one non-diffusion-weighted scan. In the Osaka 2 group, which contained 331 healthy volunteers, whole-brain axial DTI scanning was performed using a 3.0 T GE DISCOVER 750 scanner (GE Healthcare, Milwaukee, WI) using an eight-channel head, neck, and spine (HNS) coil with the following parameters: two-dimensional diffusion-weighted spin-echo EPI, TR = 15 s, TE =61.1 ms, acquisition matrix = 128 × 128, reconstruction matrix = 256 × 256, ASSET acceleration factor = 2, FOV = 240 × 240 mm, slice thickness = 2.6 mm, voxel size = 0.94 × 0.94 × 2.6 mm, number of slices = 60. A diffusion sensitization gradient was applied with 15 noncollinear gradient directions and a b value of 1000s/mm^2, in addition to one non-diffusion-weighted scan.

Table 1
Demographic characteristics and work hours of participants.

	Mean	SD
Age	30.4	13
Education (years)	14.9	1.77
Total work hours (hours/week)	37.2	18.6
Work hours in the Work for Pay category (hours/week)	12.4	19.8
Work hours in the Work at Home category (hours/week)	4.5	11.3
Work hours in the Student category (hours/week)	20.3	21.5

Mean and standard deviation (SD) in 483 participants (265 male and 218 female) is shown.

2.3. Imaging analysis

Imaging analysis was performed as previously described [13]. Briefly, DTI data were preprocessed with head motion correction and distortion correction induced by eddy current was performed using edd_correct (FSL 5.0; https://fsl.fmrib.ox.ac.uk/fsl). The DTI indices involving FA, MD, and RD were calculated using dti_fit (FSL 5.0). Tract-based spatial statistics (TBSS), using the ENIGMA-DTI template and JHU regions of interest (ROIs), was applied to extract local values (25 ROIs, see Table 2) of the DTI indices based on the ENIGMA-DTI protocols [11] (http://enigma.ini.usc.edu/protocols/dtiprotocols/).

2.4. Psychosocial measures

The number of work hours per week during the last three months was obtained using the SAA, developed by Sumiyoshi, et al. [32]. The SAA consists of Work for Pay, Work at Home, and Student categories. The Work for Pay category reflected the number of work hours for which wages were paid. The Work at Home category reflected the time spent doing housework without wages for one or more family members, not only for oneself. Finally, the Student category reflected the time spent on school-related study. If the participants were eligible for more than one category, work hours were summed across the categories, and the sum was referred to as total work hours. The SAA was conducted through interviews by psychologists or physicians.

2.5. Statistical analysis

All statistical analyses were conducted using SPSS version 26 (IBM Corp., Armonk, NY). We performed partial correlation analyses (covariates: age, sex, and MRI scanner) to investigate the associations of DTI indices with work hours. Statistical significance was defined as $p < 6.67 \times 10^{-4}$ (0.05/75, 25 ROIs × 3 DTI indices) according to the Bonferroni correction.

3. Results

We performed partial correlation analyses between total work hours and FA, RD, and MD in 483 participants (Table 2). There was no statistically significant correlation observed between FA or RD and total work hours in any of the 25 ROIs. The MD values of the anterior limb of the internal capsule (ALIC) and the superior fronto-occipital fasciculus (SFO) were negatively correlated with work hours (Fig. 1, ALIC: r = -0.192, $p = 2.3 \times 10^{-5}$; SFO: r = -0.161, $p = 3.9 \times 10^{-4}$) while the MD values of the other ROIs were not correlated with work hours. Further analyses were performed for each of the three categories of total work hours. We found that the MD values of the ALIC and the SFO were negatively correlated with work hours in the Work for Pay category (ALIC: r = -0.211, $p = 3.2 \times 10^{-6}$); SFO: r = -0.163, $p = 3.4 \times 10^{-4}$) but

Table 2
Results of the partial correlation analyses between DTI indices and total work hours.

	FA		RD		MD	
	r	*p*	*r*	*p*	*r*	*p*
Corpus callosum	0.041	3.7×10^{-1}	−0.085	6.3×10^{-2}	−0.112	1.4×10^{-2}
Genu of corpus callosum	0.016	7.3×10^{-1}	−0.067	1.4×10^{-1}	−0.122	7.6×10^{-3}
Body of corpus callosum	0.051	2.6×10^{-1}	−0.076	9.7×10^{-2}	−0.092	4.3×10^{-2}
Splenium of corpus callosum	0.018	6.9×10^{-1}	−0.078	8.6×10^{-2}	−0.091	4.6×10^{-2}
Cingulate gyrus	0.020	6.6×10^{-1}	−0.078	8.8×10^{-2}	−0.131	4.0×10^{-3}
Cingulum hippocampus	0.022	6.4×10^{-1}	−0.056	2.2×10^{-1}	−0.088	5.3×10^{-2}
Corona radiata	0.026	5.7×10^{-1}	−0.087	5.7×10^{-2}	−0.119	8.9×10^{-3}
Anterior corona radiata	0.011	8.1×10^{-1}	−0.094	4.0×10^{-2}	−0.129	4.5×10^{-3}
Posterior corona radiata	0.009	8.5×10^{-1}	−0.037	4.2×10^{-1}	−0.068	1.4×10^{-1}
Superior corona radiata	0.041	3.7×10^{-1}	−0.086	5.9×10^{-2}	−0.117	1.1×10^{-2}
Corticospinal tracts	0.000	1.0	−0.023	6.2×10^{-1}	0.002	9.7×10^{-1}
External capsule	0.008	8.6×10^{-1}	−0.097	3.3×10^{-2}	−0.138	2.5×10^{-3}
Fornix	0.001	9.7×10^{-1}	−0.012	8.0×10^{-1}	−0.016	7.2×10^{-1}
Fornix/Stria terminalis	−0.047	3.1×10^{-1}	0.026	5.7×10^{-1}	−0.022	6.4×10^{-1}
Internal capsule	−0.003	9.6×10^{-1}	−0.064	1.6×10^{-1}	−0.124	6.5×10^{-3}
Anterior limb of internal capsule	−0.014	7.6×10^{-1}	−0.107	1.9×10^{-2}	**−0.192**	**$2.3 \times 10-5$***
Posterior limb of internal capsule	0.030	5.1×10^{-1}	−0.065	1.6×10^{-1}	−0.102	2.5×10^{-2}
Inferior fronto-occipital faciculus	0.030	5.1×10^{-1}	−0.073	1.1×10^{-1}	−0.130	4.5×10^{-3}
Posterior thalamic radiation	−0.050	2.7×10^{-1}	−0.004	9.3×10^{-1}	−0.059	1.9×10^{-1}
Retrolenticular part of internal capsule	−0.025	5.8×10^{-1}	0.008	8.7×10^{-1}	−0.031	5.0×10^{-1}
Superior fronto-occipital fasciculus	−0.043	3.4×10^{-1}	−0.073	1.1×10^{-1}	**−0.161**	**$3.9 \times 10-4$***
Superior longitudinal fasciculus	−0.040	3.8×10^{-1}	−0.050	2.8×10^{-1}	−0.121	7.7×10^{-3}
Sagittal stratum	0.002	9.7×10^{-1}	−0.058	2.1×10^{-1}	−0.086	5.8×10^{-2}
Uncinate fasciculus	0.069	1.3×10^{-1}	−0.043	3.5×10^{-1}	−0.002	9.6×10^{-1}
Average of the full skeleton	0.032	4.9×10^{-1}	−0.113	1.3×10^{-2}	−0.145	1.5×10^{-3}

Legend: The mean diffusivity (MD) values of the anterior limb of the internal capsule and the superior fronto-occipital fasciculus show significant negative correlations with total work hours. * Bonferroni-corrected $p < 0.05$.
Abbreviations: DTI, diffusion tensor imaging; FA, fractional anisotropy; RD, radial diffusivity; MD, mean diffusivity.

not correlated with work hours in the Work at Home category (ALIC: $r =$ -0.028, $p =$ 0.54; SFO: $r = 0.014$, $p =$ 0.77) or the Student category (ALIC: $r = 0.021$, $p =$ 0.65; SFO: $r =$ -0.016, $p =$ 0.73).

4. Discussion

In this study, the MD values of the ALIC and the SFO were negatively correlated with work hours. Further analyses revealed that the MD values of the ALIC and the SFO were negatively correlated specifically with work hours in the Work for Pay category. On the other hand, the FA values of the ALIC and SFO were not correlated with work hours. These results suggest that the MD values decreased while maintaining the ratio of three eigenvalues. These findings indicate an association between the time commitment to paid work and the subtle change in the microstructure of the ALIC and SFO cerebral white matter. In addition, the significant correlations between the MD value of SFO and work hours did not remain after adding years of education to the covariates ($r =$ -0.152, $p = 8.3 \times 10^{-4}$). The MD value of SFO and working hours may be somewhat related, but their correlation may be weak. In contrast, the significant correlations between the MD value of ALIC and work hours remained even after adding years of education to the covariates ($r =$ -0.176, $p = 1.1 \times 10^{-4}$).

The ALIC carries fibers connecting the frontal lobe and the thalamus and brainstem [26]. The thalamic and brainstem fibers from the frontal lobe are related to emotions, motivation, cognition, and decision making [9,25]. Furthermore, the ALIC is a target site for stereotaxic surgery, such as deep brain stimulation (DBS) for obsessive-compulsive disorder [8], and is also being clinically studied as a target site for neurosurgical treatment of treatment-resistant depression [4]. Decreased MD values of ALIC might lead to increased emotion, proper motivation, adequate cognition, and good decision making as well as reduced irrational compulsiveness and depression, eventually resulting in increased participation in jobs, i.e., increased work hours in the Work for Pay category.

The specifics of the SFO nerve fiber bundles are still controversial [3,17]. One study argues that the SFO is a fiber tract around the superior thalamic peduncle, inferior thalamic peduncle, and stria terminalis [17]. In contrast, other studies have reported that the SFO is an association fiber tract that connects the frontal lobe and parietal lobe and is considered a visual processing pathway [5] or a spatial recognition pathway [35]. The SFO is reportedly associated with impaired visual processing in alcoholic patients [2] and with acute spatial neglect [10]. Interestingly, the length of work hours is also known to be correlated with eye movements during the free-viewing that are closely related to visual explorations [18,21]. Thus, decreased MD values of SFO might be correlated with the length of work hours in relation to visual and spatial recognition. However, this is difficult to conclude because there are no data on whether the work content is of a type related to visual spatial recognition.

Among the social activities that we examined, work time in the Work for Pay category but not in the Work at Home or Student category was significantly correlated with the MD values of the ALIC and the SFO. Although this result cannot be said to be definitive due to a lack of data for each type of work, it might suggest that the demands placed on the brain circuitry by the Work for Pay category are different from those imposed by the Work at Home and Student categories. These different categories of work might differ in the type of motivation. For example, the work classified in the Work for Pay category tends to be an unavoidable activity that depends on external motivations such as the economic need to support one's household budget. On the other hand, salary-free housework, i.e., the work classified in the Work at Home category, likely depends not only on external motives but also on internal motives such as compassion for one's family members, especially one's children. The work classified in the Student category is likely driven by internal motives and/or by expectations of others. Thus, the association between the MD values of the ALIC and the SFO might depend on the type of motivation.

There is a possibility that white matter microstructure is affected by working conditions within three months. A study reported correlations between grey matter volumes and daily activities within one year [36]. However, there is no direct evidence of whether working conditions over the lifespan or acute working conditions affect white matter

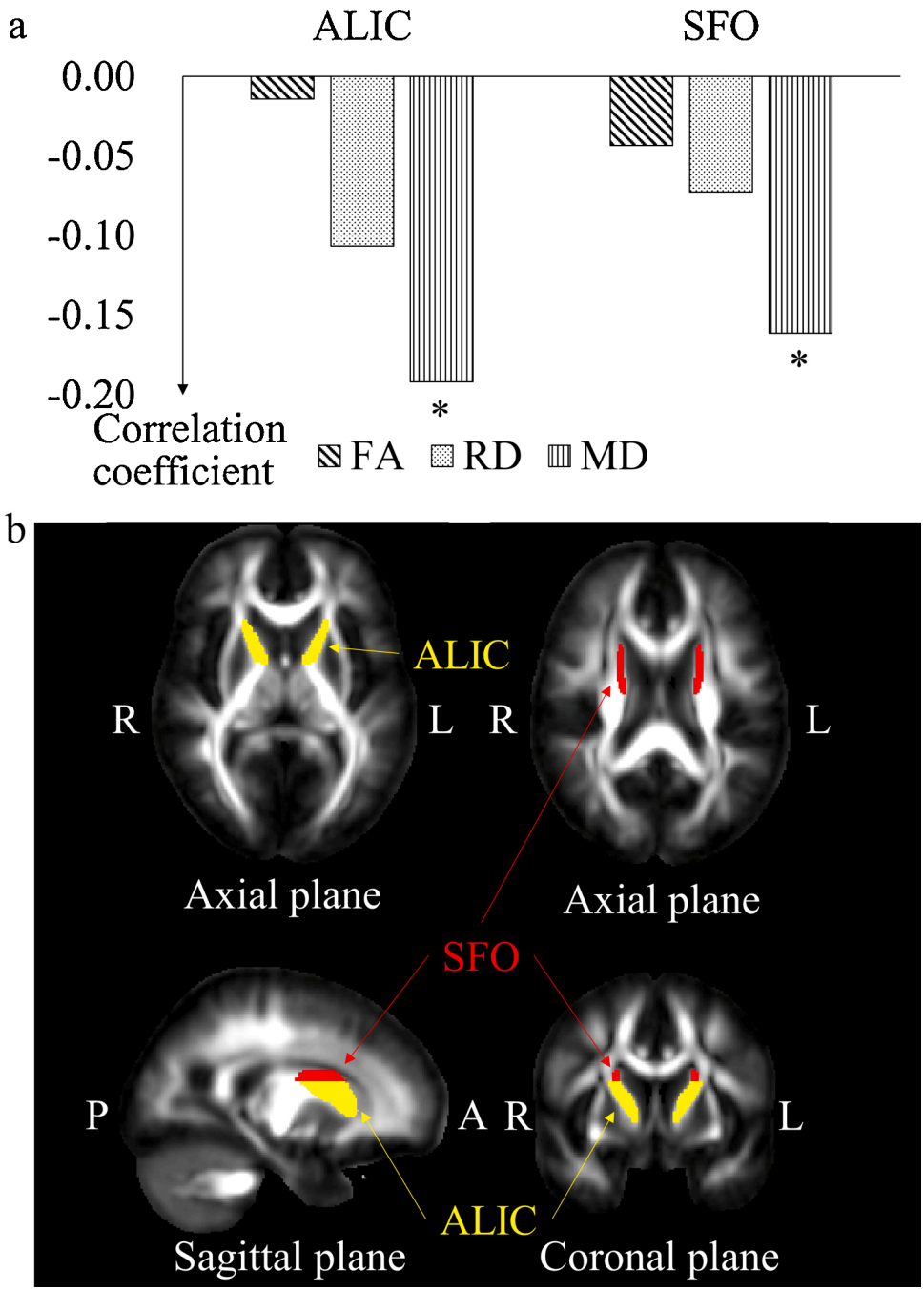

Fig. 1. The correlations between total work hours and DTI indices in the anterior limb of the internal capsule (ALIC) and the superior fronto-occipital fasciculus (SFO). (a) The correlation coefficients between work hours and the fractional anisotropy (FA), radial diffusivity (RD), and mean diffusivity (MD) of the ALIC and SFO. The MD values of the ALIC and the SFO were significantly correlated with total work hours. * Bonferroni-corrected $P < 0.05$. (b) Views of the ALIC and the SFO in the axial, sagittal, and coronal planes.
Abbreviations: ALIC, anterior limb of internal capsule; SFO, superior fronto-occipital fasciculus; FA, fractional anisotropy; RD, radial diffusivity; MD, mean diffusivity; R, right; L, left; P, posterior; A, anterior; DTI, diffusion tensor imaging.

microstructure. This is a major limitation of this study. In future studies, the time span of working conditions that affect white matter microstructure should be examined.

5. Conclusion

In the present study, we investigated whether there are significant associations between social activity and DTI indices of white matter connectivity. We found that the MD values of the ALIC and the SFO were negatively correlated with total work hours and specifically with hours in the Work for Pay category. Thus, we conclude that the connectivity between brain regions, similar to the volumes of specific brain regions, is related to social activities in a manner that depends on the type of work.

CRediT authorship contribution statement

Junya Matsumoto: Conceptualization, Data curation, Formal analysis, Visualization, Writing - original draft, Writing - review & editing. **Masaki Fukunaga:** Software, Data curation, Visualization. **Kenichiro Miura:** Validation, Formal analysis, Software, Data curation, Writing - review & editing. **Kiyotaka Nemoto:** Formal analysis, Software, Data curation. **Daisuke Koshiyama:** Software, Formal analysis, Investigation, Data curation. **Naohiro Okada:** Formal analysis, Investigation, Data curation. **Kentaro Morita:** Formal analysis, Investigation, Data curation. **Hidenaga Yamamori:** Resources, Investigation, Methodology, Data curation. **Yuka Yasuda:** Resources, Investigation, Methodology, Data curation. **Michiko Fujimoto:** Resources, Investigation, Methodology, Data curation. **Naomi Hasegawa:** Validation, Writing - review & editing. **Yoshiyuki Watanabe:** Data curation, Methodology,

Investigation, Resources. **Kiyoto Kasai:** Formal analysis, Investigation, Data curation. **Ryota Hashimoto:** Conceptualization, Methodology, Validation, Investigation, Resources, Data curation, Writing - review & editing, Supervision, Project administration, Funding acquisition.

Declaration of Competing Interest

All the authors declare that they have no conflicts of interest related to this project.

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