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Original Article

## Assessing structural and functional connectivity in the ipsilesional precentral gyrus using 1.5 T MRI in patients with stroke and the relationships between functional and structural connectivity and motor function

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**Abstract.** [Purpose] The purpose of this study was to determine a method for analyzing functional connectivity in patients with stroke using 1.5 T magnetic resonance imaging (MRI) and to examine the relationships between functional and structural connectivity and motor function. [Subjects and Methods] Five patients with stroke (4 men and 1 woman; mean age  $\pm$  standard deviation [SD]: 54.6  $\pm$  16.8 years) and 5 healthy participants (4 men and 1 woman; mean age  $\pm$  SD: 28.8  $\pm$  2.2 years) were included. The functional connectivity between the ipsilateral precentral gyrus and the contralateral precentral gyrus (preCG), postcentral gyrus (postCG), supplementary motor area (SMA), and thalamus was investigated using 1.5 T MRI. In addition, the volume ratio of both corticospinal tracts (rTV) was determined using diffusion tensor tractography. [Results] Healthy participants had strong functional connectivity with the contralateral cortical preCG, postCG, and SMA. Patients with stroke had functional connectivity similar to that of healthy participants, although weaker. In addition, patients with high rTV had good motor function and strong functional connectivity. [Conclusion] This study provides a method for analyzing functional and structural connectivity in patients with stroke using 1.5 T MRI.

Key Words: ipsilesional precentral gyrus, functional connectivity, 1.5 T MRI

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### 1. INTRODUCTION

Resting state functional magnetic resonance imaging (rsfMRI) was recently developed as a method for analyzing brain function in patients with stroke. In rsfMRI, the fluctuation component of the blood-oxygen-level dependent (BOLD) signal at rest is extracted, and the temporal correlations between brain regions are calculated. The correlation between anatomically distinct regions represents functional connectivity (FC) in the brain<sup>1</sup>). Conventional task-based fMRI has limitations in that preparing experimental tasks is necessary and that these tasks must be executed within the MRI field. However, in the case of rsfMRI, patients are in a state of rest in the MRI field and tasks are unnecessary, making rsfMRI

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easy to use for analyzing the brain function of patients with stroke. Previous studies have reported that the motor networks in the brain are the primary motor cortex (M1), premotor cortex, supplementary motor area (SMA), and subcortical areas, such as the basal ganglia, thalamus, and cerebellum<sup>2,3</sup>). Furthermore, it has been reported that motor network activity in patients with stroke changes bilaterally compared to that in healthy individuals, and in particular, the FC of the contralesional cortex suggests the possibility of effecting motor function recovery<sup>4-10</sup>). Previous studies using rsfMRI used 3 T MRI<sup>5-10</sup>). However, although 3 T MRI offers the advantage of producing high-resolution data, it is very expensive, and not all hospitals have access to it. In contrast, diffusion tensor tractography (DTT) is most commonly used for analyzing the structural connectivity (SC) of the brain using MRI. DTT is a method of visualizing white matter using diffusion tensor imaging (DTI), and many researchers have reported the relationship between DTT and motor function of the corticospinal tract (CST) in patients with stroke<sup>11-13</sup>). Therefore, developing a method for assessing FC using 1.5 T MRI and for assessing SC using DTT would enable many hospitals to perform analyses on the relationship between the FC and SC of the ipsilesional motor cortex in patients with stroke. This ability would in turn accelerate data accumulation that could be used to help determine optimal rehabilitation for patients with stroke. This pilot study provides a method for assessing FC in patients with stroke using 1.5 T MRI and examines the relationship between FC and SC and motor function.

## 2. SUBJECTS AND METHODS

### 2.1 Subjects

This study included 5 patients with stroke who were admitted to Sakura Jyuji Fukuoka Hospital (4 men and 1 woman; mean age  $\pm$  standard deviation [SD]:  $54.6 \pm 16.8$  years) and 5 healthy participants (4 men and 1 woman; mean age  $\pm$  SD:  $28.8 \pm 2.2$  years) (Table 1). All patients had experienced cerebral hemorrhage; 3 had lesions in the putamen and 2 had lesions in the thalamus. Patients were classified into 2 groups (mild and serious) based on their having a Brunnstrom recovery stage of III or lower, respectively, and were also classified according to functional ambulation categories. All participants were right-handed. The hospital's ethics review board approved this study (No. 2016090502), and informed consent was obtained from all participants prior to their participation in the study.

### 2.2 Methods

A 1.5 T MRI scanner (Brivo; GE Healthcare, Hino, Tokyo, Japan) was used for rsfMRI and 3-dimensional T1-weighted imaging (3DT1) and DTI. The rsfMRI images were acquired using gradient echo echo-planar imaging (EPI) with the following parameters: repetition time (TR), 2500 ms; echo time (TE), 50 ms; slice thickness, 3.2 mm; spacing, 0.8 mm; field of view (FOV),  $21.2 \times 21.2$  cm; matrix size,  $64 \times 64$ ; scan, axial; volume, 200; slice order, ascending sequential; and total scan time, 16 min 40 s. Before rsfMRI scanning, all participants were instructed to stay still, think of nothing in particular, keep their eyes opened, and stay awake during scanning. 3DT1 images were acquired using gradient echo fast spoiled gradient (SPGR) with the following parameters: TR, 12.3 ms; TE, 5.2 ms; slice thickness, 3.2 mm; FOV,  $21.2 \times 21.2$  cm; matrix size,  $256 \times 256$ ; and total scan time, 10 min 09 s. DTI images were acquired using single-shot EPI with the following parameters: TR, 9000 ms; TE, 102.59 ms; slice thickness, 5.0 mm; FOV,  $24.0 \times 24.0$  cm; matrix size,  $128 \times 128$ ; b-value, 1000 s/mm<sup>2</sup>; motion probing gradient (MPG), 15 directions; and total scan time, 4 min 57 s. Preprocessing for FC analysis included processing the functional images (i.e., rsfMRI) and the structural images (i.e., 3DT1) using MATLAB-based SPM 12<sup>14</sup>) and CONN<sup>15</sup>). Preprocessing of functional images included realignment, center-to-coordinate alignment, slice timing correction, normalization, outlier detection, and smoothing. Furthermore, preprocessing of structural images included center-to-coordinate alignment, segmentation, and normalization. After preprocessing, the FC between the ipsilesional precentral gyrus (preCG) and contralesional preCG, postcentral gyrus (postCG), SMA, and thalamus in patients with stroke was calculated. The seed region of interest (ROI) for healthy participants was the preCG of the left-side cortex. All FC analysis protocols and detailed descriptions of the calculations used are freely available<sup>15</sup>). In addition, DSI studio<sup>16</sup>) was used for SC analysis, and DTI images were used to visualize bilateral CSTs. The ROI of the CST was the cerebral peduncle in a slice of the midbrain with the following tracking algorithm: streamline algorithm, FA threshold 0.1, angle threshold 60°, and step size 1 mm. Finally, the volume ratio (ratio of the tract volume [rTV]) of the contralesional CST to ipsilesional CST) was calculated.

Table 1. Demographic and clinical characteristics of the subjects and result of functional connectivity and structural connectivity

Subject	Gender	Age (years)	Type of stroke	Lesion side	Post stroke (weeks)	Brunnstrom stage			FAC	M-FIM	Z value			rTV	
						Upper	Hand	Lower			PreCG	PostCG	SMA		Thalamus
<b>Patients with stroke</b>															
1	M	79	putamen	Lt	9	II	II	II	1	17	0.29	0.25	-0.01	0.17	0.49
2	F	34	putamen	Rt	4	II	II	II	1	30	0.20	0.37	-0.02	0.03	0.40
3	M	54	thalamus	Rt	3	V	VI	V	4	67	1.21	1.06	0.69	-0.13	0.75
4	M	46	putamen	Lt	24	IV	IV	V	4	86	0.86	0.63	0.36	-0.30	0.61
5	M	60	thalamus	Lt	16	V	V	V	5	88	0.82	0.78	0.51	-0.08	1.03
Mean ± SD	M=4,F=1	54.6 ± 16.8			11.2 ± 8.8					57.6 ± 29.1	0.67 ± 0.38	0.62 ± 0.29	0.31 ± 0.28	-0.06 ± 0.16	0.66 ± 0.25
<b>Healthy participants</b>															
6	M	27	-	-	-	-	-	-	-	-	1.05	0.68	0.87	-0.26	1.05
7	M	31	-	-	-	-	-	-	-	-	1.51	0.86	0.15	0.01	0.99
8	F	30	-	-	-	-	-	-	-	-	1.30	1.06	0.76	-0.23	0.91
9	M	26	-	-	-	-	-	-	-	-	0.95	0.58	0.81	-0.51	1.23
10	M	30	-	-	-	-	-	-	-	-	1.27	0.90	0.56	-0.38	1.08
Mean ± SD	M=4,F=1	28.8 ± 2.2									1.22 ± 0.20	0.82 ± 0.17	0.63 ± 0.26	-0.27 ± 0.17	1.05 ± 0.1

FAC: Functional Ambulation Categories, M-FIM: Motor score of Functional Independence Measure, PreCG:precentral gyrus, PostCG: postcentral gyrus, SMA: supplementary motor area, rTV: ratio of tract (corticospinal tract) volume

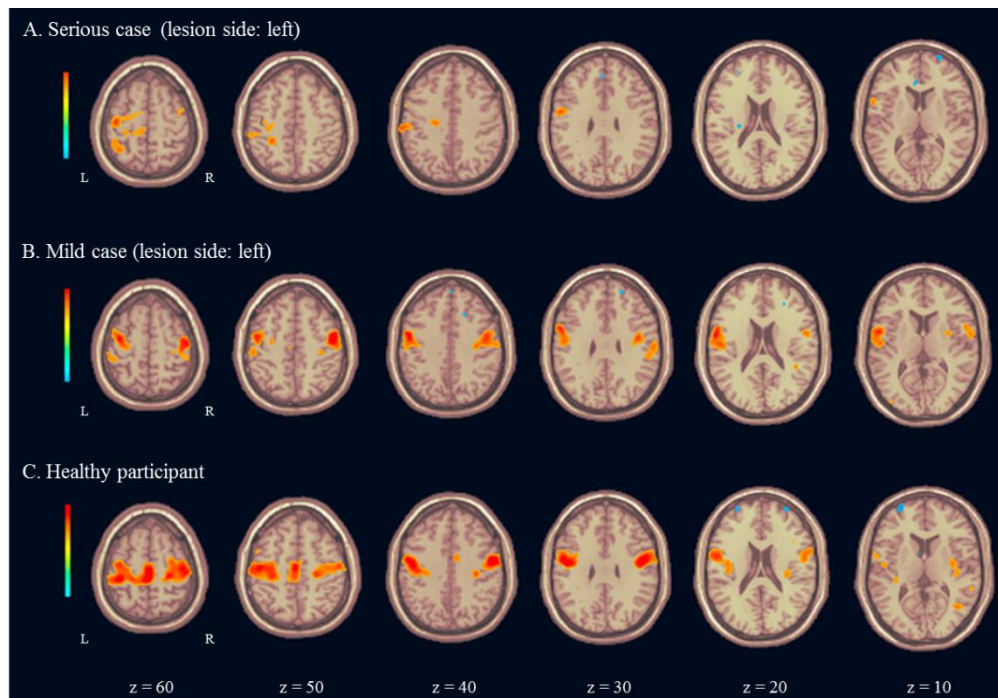


Figure 1. Result of the FC between the ipsilesional precentral gyrus and the whole brain (threshold of correlation coefficient: 0.4). The seed region of interest of healthy participants was precentral gyrus of the left side cortex.

### 3. RESULTS

The FC analysis revealed strong connectivity with the preCG, postCG, and SMA of the contralateral cortex in healthy participants (Table 1 and Figure 1). Patients in the mild group showed connectivity between the ipsilesional preCG and contralesional preCG, postCG, and SMA, similar to that in healthy participants; however, the connectivity strength was attenuated. In addition, patients in the serious group also showed connectivity between contralesional preCG, postCG, and SMA, but the strength of this connectivity was even further attenuated. The rTV values among healthy participants, patients in the mild group, and patients in the serious group were  $1.03 \pm 0.12$ ,  $0.76 \pm 0.19$ , and  $0.45 \pm 0.06$ , respectively. Patients with high rTV had good motor function and strong FC.

### 4. DISCUSSION

This pilot study aimed to provide a method for determining and analyzing FC using 1.5 T MRI. FC involves focusing on the temporal correlation of the low-frequency component (<0.08 Hz) of the BOLD signal at rest, and fluctuation at rest is believed to reflect the baseline activity of nerve cells<sup>17,18</sup>. In earlier studies on FC using 3 T MRI, TR was kept consistent in the range of 2000–3000 ms, and TE, flip angle, and slice thickness were regulated according to TR. However, the scan time and the volume varied, and although a scan time of 5 minutes and a volume of 120 is reportedly adequate<sup>1</sup>, a report suggests that reliability significantly improves when the scan time is increased to 13 minutes<sup>19</sup>. A longer scan time increases stress on participants (e.g., thinking of nothing in particular, keeping eyes opened, and staying awake during scanning). Although the scan time and volume depend on MRI performance, a longer scan time has been reported to be preferable for examining the treatment effect longitudinally. Therefore, because of the use of 1.5 T MRI in this study, the scan time was set to 16 min 40 s and the volume to 200. Furthermore, FC is known to be attenuated when eyes are kept closed, in contrast to when they are kept open<sup>20</sup>. Therefore, in this study, scans were performed with the participants keeping their eyes open. Moreover, to analyze the frequency in the resting state, the images of the initial scan were excluded and analyzed. As a result, FCs were observed in contralesional preCG, postCG, and SMA in healthy participants, a finding consistent with that of several previous studies using 3 T MRI<sup>7-10</sup>. The results show

that FC can be analyzed using 1.5 T MRI by increasing the scan time and volume. Patients with stroke had FC of attenuated strength in contralesional preCG, postCG, and SMA; the attenuation was more pronounced in patients in the serious group than in patients in the mild group. The results of this study are consistent with those of previous studies that used 3 T MRI<sup>21-23)</sup> in that patients with stroke were found to have decreased FC in contralesional M1 and SMA compared to that in healthy participants. Furthermore, the decreased FC suggests disruption of harmonious interactions between the bilateral M1s<sup>24)</sup>, which is believed to be strongly associated with motor function in patients with stroke<sup>7,9)</sup>. The results of this study show that the FC of patients with extensive motor impairment was lower than that of those with milder impairment. The DTT of CST was used for the analysis of SC of the preCG. In DTT, fibers are tracked using FA obtained by DTI, but FA is influenced by the imaging parameters of DTI. Therefore, it is necessary to acquire high-quality DTI. However, DTI data are dependent on MRI hardware configuration, available scanning time, and the specific anatomic structures to be investigated<sup>25)</sup>. For these reasons, there is no consensus on the best DTI imaging parameters to use for clinical studies. The use of multiple MPGs for diffusion tensor estimation is recommended, and a study suggested that 30 directions are necessary to acquire robust data<sup>26)</sup>. However, the increase in MPG has the disadvantage of requiring a long scan time. Therefore, the MPG was set to 15 directions in this study, considering the feasibility of replication in clinical studies in many hospitals. Another study suggested that FA with minimal errors can be acquired using an MPG of 15 directions<sup>27)</sup>. Hence, the quality of DTIs in this study seems adequate. In addition, 2 important parameters that affect the results of DTT are FA and angle thresholds. FA and angle thresholds are criteria for stopping fiber tracking in DTT, and typical FA and angle thresholds used for the adult brain range from 0.1 to 0.3 and 40° to 70°, respectively. For DTIs obtained with a high signal-to-noise ratio acquired using 3 T MRI or an MPG of >30 directions, a very low FA can yield more spurious fibers (i.e., false-positives). However, because this study used 1.5 T MRI and an MPG of 15 directions, the FA threshold was set to 0.1. The angle threshold was set to 60°, which is in line with several previous studies<sup>28-30)</sup> on DTT for CST. The results of this study showed that patients with higher rTVs tended to have better motor function. Because the completeness of CST decisively affects the recovery of motor function in patients with stroke, the results of this study are consistent with those of previous studies<sup>11-13, 28-30)</sup>. In addition, FC in contralesional preCG, postCG, and SMA was observed in patients with higher rTVs, indicating that the rTV of the CST might be related to FC in these regions.

This study has limitations. The first is the small sample size. Further studies with larger samples are required to draw definitive conclusions on the relationship between FC and SC and motor function. Second, the study did not assess long-term data. According to previous studies that used task-based fMRI, brain activity after stroke shifts to the contralesional cortex, recruits additional regions that are not activated in healthy individuals, and then progresses to the ipsilesional cortex<sup>31-33)</sup>. Therefore, a longitudinal study of the relationship between FC and SC is needed.

In conclusion, this study provides a method for analyzing FC and SC in patients with stroke using 1.5 T MRI. This method could enable many more hospitals to study FC and SC longitudinally, which would help accumulate data for determining appropriate rehabilitation of patients with stroke.

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No funding was provided for this study.

#### **Conflict of interest**

The authors declare no conflicts of interest.

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Original Article

## Cross-sectional survey of physical therapy students associated with overseas volunteers

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**Abstract.** [Purpose]The purpose of this study was to evaluate the differences in interest, reasons, and benefits among undergraduate grade levels, associated with overseas volunteer participation in physical therapy students using a cross-sectional survey.  
[Subjects and methods] Three hundred and fifty-seven physical therapy students, enrolled at the International University of Health and Welfare's Ohtawara campus in 2017, participated in this study. A cross-sectional design was used to study differences among undergraduate grade levels in physical therapy students. The degree of interest, reasons, and benefits, associated with overseas volunteer participation was evaluated by a questionnaire survey using a four-point scale.  
[Results] Concerning the reason for overseas volunteer participation, significant differences were found in five items; regarding benefits, significant differences were found in four items.  
[Conclusion] It was suggested that we need to encourage students to engage in overseas volunteer participation from the time of admission.  
Key Words: overseas volunteer, physical therapy students, questionnaire survey

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### 1. INTRODUCTION

In recent years, global health has been interested in medical education<sup>1-3)</sup>. However, there are very few research reports from medical professionals associated with rehabilitation, such as physical therapists, occupational therapists, or speech therapists, regarding interest in overseas volunteer participation. These reports were described by the Japan Overseas Cooperation Volunteers in the Japan International Cooperation Agency<sup>4,5)</sup>.

The subject A State of Health and Welfare in Foreign Countries has been established at the International University of Health and Welfare's Ohtawara campus. Students who have taken this course at second grade stay in a foreign country for about two weeks during periods of vacation. It is necessary to understand the differences in grades for interests in overseas volunteer participation.

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Therefore, the purpose of this study was to evaluate the interest, reasons, and benefits among undergraduate grade levels, associated with overseas volunteer participation in physical therapy students using a cross-sectional survey.

## 2. SUBJECTS AND METHODS

Three hundred and fifty-seven physical therapy students, enrolled at the International University of Health and Welfare's Otawara campus in 2017, participated in this study. There were ninety students from the first grade (age= 18.6±0.7 [years mean ± SD]), seventy-four from the second grade (age= 19.7±1.6years), ninety-nine from the third grade (age= 20.7±1.0years), and ninety-four from the fourth grade (age= 21.7±1.0years). There were one hundred and ninety male, and one hundred and sixty-seven female students.

Twenty-three students were excluded because of a lack of informed consent and absence. The study was approved by the institutional review board of the corresponding author's university (Approval No.2017-Ig-7).

A cross-sectional design was used to study differences among undergraduate grade levels in physical therapy students. Interest, reasons, and benefits, associated with overseas volunteer participation were evaluated by a questionnaire survey using a four-point scale. Surveys were set for each grade in late September.

The subjects checked one option from a four-point scale depending on whether they were "very interested," "quite interested," "not very interested," or "not at all interested," and were investigated the degree of interest in overseas volunteer participation.

For students participating in the overseas volunteer program, the survey offered eight reasons which could be selected: 1) I want to try it for myself: 2) I was invited by a friend or acquaintance: 3) I want to help people: 4) I want to understand a different culture: 5) I want to study society: 6) I want to protect the environment or cultural properties: 7) I want to make it advantageous for employment or admission: and 8) I want to acquire language skills. For students who had participated in the overseas volunteer program, the survey offered eight benefits which could be selected: 1) language skills: 2) spirit of challenge: 3) personal connections: 4) confidence: 5) objective viewpoint in comparison to my own country: 6) understanding a different culture: 7) new sense of value: and 8) direction of course after graduation. The participants checked one option from a four-point scale which represented whether they "Strongly agree," "Agree," "Disagree," or "Strongly disagree."

The data were analyzed using descriptive statistics and a  $\chi^2$  test using SPSS for Windows (22.0 IBM Corporation). P values < 0.05 indicated statistical significance.

## 3. RESULTS

For the degree of interest in overseas volunteer participation, "very interested" was 12.1%, "quite interested" was 45.8%, "not very interested" was 37.3%, and "not at all interested" was 4.8%. No significant difference was found among grades.

In the reason for overseas volunteer participation, significant differences were found in five items: 2) I was invited by a friend or acquaintance: 3) I want to help people: 4) I want to understand a different culture: 7) I want to make it advantageous for employment or admission: and 8) I want to acquire language skills (Table 1).

Regarding benefits for overseas volunteer participation, significant differences were found in four items: 2) spirit of challenge: 4) confidence: 5) objective viewpoint in comparison to my own country: and 8) direction of course after graduation (Table 2).

Table 1 Reasons among undergraduate grade levels(%)

<Reason>	Strongly agree	Agree	Disagree	Strongly disagree	
I want to try it for myself					
1st	14	53	29	4	
2nd	22	53	23	2	
3rd	13	39	40	7	
4th	11	50	37	2	
total	15	48	33	4	
I was invited by a friend or acquaintance					
1st	7	31	49	13	*
2nd	5	40	50	5	
3rd	2	30	48	20	
4th	2	29	64	5	
total	4	32	53	11	
I want to help people					
1st	37	45	16	2	*
2nd	19	60	20	1	
3rd	11	64	21	4	
4th	14	67	19	0	
total	20	59	19	2	
I want to understand a different culture					
1st	39	49	10	2	*
2nd	28	56	15	1	
3rd	19	54	21	6	
4th	17	62	20	1	
total	25	55	17	3	
I want to study society					
1st	28	54	15	3	
2nd	23	60	16	1	
3rd	13	64	17	6	
4th	19	65	16	0	
total	20	61	16	3	
I want to protect the environment or cultural properties					
1st	13	47	36	4	
2nd	9	51	37	3	
3rd	5	40	46	9	
4th	7	55	37	1	
total	8	48	39	5	
I want to make advantageous for employment or admission					
1st	20	51	22	7	*
2nd	12	49	38	1	
3rd	5	35	47	13	
4th	6	47	47	1	
total	11	45	38	6	
I want to acquire language skills					
1st	34	39	25	2	*
2nd	27	48	24	1	
3rd	19	50	23	8	
4th	17	57	24	2	
total	24	48	24	4	

\*p<0.05

Table2 Benefits among undergraduate grade levels(%)

<Benefit>	Strongly agree	Agree	Disagree	Strongly disagree	
Language skills					
1st	45	48	5	2	
2nd	38	58	4	0	
3rd	38	55	7	0	
4th	31	60	8	1	
total	38	55	6	1	
Spirit of challenge					
1st	48	47	3	2	*
2nd	56	42	2	0	
3rd	35	61	4	0	
4th	34	61	5	0	
total	42	53	4	1	
Personal connections					
1st	37	53	7	3	
2nd	36	58	6	0	
3rd	26	64	10	0	
4th	25	62	13	0	
total	31	59	9	1	
Confidence					
1st	41	52	5	2	*
2nd	49	46	5	0	
3rd	28	59	13	0	
4th	27	65	8	0	
total	35	56	8	1	
Objective viewpoint in comparison to my own country					
1st	33	56	8	3	*
2nd	38	57	5	0	
3rd	21	65	14	0	
4th	22	66	12	0	
total	28	61	10	1	
Understanding a different culture					
1st	41	53	3	3	
2nd	44	52	4	0	
3rd	34	56	10	0	
4th	27	62	11	0	
total	36	56	7	1	
New sense of value					
1st	33	59	6	2	
2nd	40	54	6	0	
3rd	28	61	11	0	
4th	25	66	9	0	
total	31	60	8	1	
Direction of course after graduation					
1st	23	48	28	1	*
2nd	21	60	19	0	
3rd	11	53	34	2	
4th	4	61	28	1	
total	14	57	28	1	

\*p&lt;0.05

#### 4. DISCUSSION

The sum of the results of “very interested” and “interested” demonstrated that about 60% of students were interested in overseas volunteer participation. However, no significant difference was found among grades.

Responses concerning the reasons for overseas volunteer participation tended to be aggressive. Significant differences were found in five items. This tendency is conspicuous in lower grades, such as the first and second grades.

In responses concerning the benefits of overseas volunteer participation, significant differences were found in four items. Many positive answers regarding the reasons were also remarkable for lower grade students. Though no significant difference was found among grades for participating overseas volunteers, significant differences may occur in aggressiveness and affirmation because higher grade students who have advanced to third and fourth grade acquire expertise-specific knowledge and skills, preparation for clinical practice, and employment-related activities. Therefore, we need to encourage students to engage in overseas volunteer participation from the time of admission.

This study was limited in that the participants were only from one campus. Further studies are needed to include a wider range of subjects and other schools.

All authors report that they have no conflicts of interest in this work.

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Original Article

## The Influences of Low Back Pain and Social Networking on the Health-related Quality of Life of Family Caregivers in China

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**Abstract.** [Purpose] This study investigated the prevalence of low back pain among family caregivers in China and clarified the influences of low back pain and social networking category types on health-related quality of life of caregivers. [Subjects and Methods] Data were collected from 74 subjects. Low back pain was diagnosed by physicians. A questionnaire survey was carried out to collect data on social networking, health-related quality of life, etc. [Results] The low back pain prevalence was higher than the Chinese average reported previously for those over 50 years of age. For the low back pain group, the number of categories for "in-person meetings with others" was significantly related to their health-related quality of life. According to the results of the multiple regression analysis, low back pain had the greatest impact on the health-related quality of life of family caregivers. [Conclusion] Some of the social networking activities are important for the health-related quality of life of family caregivers in China. This study also suggests that the low back pain might be the most important factor influencing the health-related quality of life.

Key words: Low back pain, social networking, health-related quality of life

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### 1. INTRODUCTION

Caregiving is generally considered strenuous; in particular, Theilmeier et al. reported that caregiving involves activities that exert stress on the lumbar spine, which can easily lead to low back pain (LBP)<sup>1</sup>. Prior research has confirmed that LBP occurs in 66.9% of employed caregivers after they start working, with 75.1% of these cases occurring during the first year of employment<sup>2</sup>. The more serious the symptoms affecting the activities of daily life (ADL) of patients receiving care, the greater the amount of care that must be provided. This is considered to make caregivers more prone to experiencing LBP<sup>3, 4</sup>. Further,

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providing care for long periods of time is known to take a particularly heavy toll on the physical and mental health of the caregivers<sup>5), 6)</sup>. For example, in a study on mothers of children with cerebral palsy, Kaya et al. found that LBP leads to the deterioration of the health-related quality of life (HRQOL)<sup>7)</sup>. Thus, measures to prevent caregiving-related LBP and interventions to treat LBP when it occurs are required. However, in over 85% of the cases, LBP is “non-specific”; that is, its causes are unclear<sup>8)</sup>. Nevertheless, chronification of non-specific LBP has been reported to be associated with psychological strain and psychosocial factors such as depression<sup>9), 10), 11)</sup>. A recent study identified a relationship between LBP and decreased gray matter in the dorsolateral prefrontal cortex (DLPFC)<sup>12)</sup>, while other studies have shown that chronification may occur as a result of inhibition by depression or anxiety of DLPFC functioning related to the attenuation of pain<sup>13), 14)</sup>. Further, in a study of male subjects aged 65 years and older in Sweden, Isacson et al. reported a significant relationship between LBP and a reduction in social network indicators after retirement<sup>15)</sup>. In another study of caregivers of immediate family members receiving home care under Brazil’s Home Care Program, Yamashita et al. found that caregivers suffering from symptom of pain in some part of the body formed numerous connections with relatives they could trust and used these connections to help mitigate their pain<sup>16)</sup>.

In Chinese hospitals, patient care is generally provided by the immediate family<sup>17)</sup>. In a study by Yan et al. of family caregivers of stroke patients, the mean age of the subjects was 56.0 years, who, on an average, provided care for over eight hours per day<sup>18)</sup>. While the prevalence rate of LBP in Chinese individuals over 50 years has been determined to be 22%<sup>19)</sup>, no prior research exists on LBP in Chinese family caregivers.

The burden of care experienced by the immediate family of a patient is influenced by various factors, such as the age of the caregiver, duration of care provided per day, amount of assistance the patient requires for ADL, and the level of support received from others<sup>16)</sup>. With such long hours of care provision, Chinese family caregivers may find it difficult to make social connections with others. This is a concern, given that in a study of elderly local residents, Lei et al. found lower HRQOL in subjects who had lesser contact with neighbors, relatives, or friends<sup>20)</sup>. Another study clarified that decline in social networking is related to depression<sup>21)</sup>.

In China, the number of Internet and smartphone users continues to increase<sup>22)</sup>. They usually use online social medias as well<sup>19)</sup>. This suggests that people’s social networks are becoming more diverse and their social relationships may be changing. In June 2016, there were approximately 710 million Internet users in China, with approximately 656 million accessing the Internet from their cellphones<sup>19)</sup>. The utilization rates of social media applications We Chat and Sina Weibo in China, have been reported to be 78.7% and 34%, respectively<sup>19)</sup>. Nevertheless, as humans ordinarily use non-verbal communication along with language to coordinate interpersonal relationships, online verbal and non-verbal communications may be insufficient<sup>20)</sup>. The study on social networks by Isacson et al. described above was published before the wide availability of the Internet, and the study by Lei et al. on HRQOL and social networks did not consider Internet-related factors<sup>18)</sup>. Thus, despite the changes in social networking due to Internet and social media, no research has examined how social networking, including the use of social media, may relate to the LBP and HRQOL of the family caregivers.

This study, therefore, aimed to clarify the incidence rates of LBP among family members who provide in-hospital care. It also sought to ascertain the impacts of LBP as well as social-media types and usage methods on HRQOL.

## **2. SUBJECTS AND METHODS**

This cross-sectional study was conducted from November 9, 2015, to January 9, 2017. The potential subjects were 101 family caregivers of patients at the Second Affiliated Hospital of the Shandong University of Traditional Chinese Medicine in China. These patients were hospitalized with varying afflictions, including acute or chronic stroke, head trauma, spinal cord injuries, and Alzheimer’s disease. All the participating caregivers and patients provided informed consent that conformed to the principles of the Declaration of Helsinki. The study was conducted with the approval of both the hospital and the

research ethics review board of Miyagi University (Miyagi University-447). To be eligible to participate, caregivers were required to be “family,” that is, an immediate family member or relative of the patient and have a good understanding of Chinese. Exclusion criteria included the following: a history of any medical condition (including cerebrovascular disease, Parkinson’s disease, amyotrophic lateral sclerosis, Alzheimer’s disease) that could hinder their ability to provide care to the patient, use of an artificial limb, or being a nurse or hired caregiver. A total of 74 caregivers (36 males and 38 females) met the inclusion criteria. The mean age of the subjects was  $46.2 \pm 9.6$  years.

Data were collected from the caregivers using a questionnaire, which included age, gender, height, weight, relationship with the patient, duration of care, time spent caring for the patient each day, the EuroQOL-5 dimensions (EQ-5D) score, and questions about social networking. The EQ-5D assesses health status with regard to five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. From these measures, an index value (“EQ-5D score”) is calculated<sup>23</sup>.

Regarding social networks, we inquired about the categories of social connections in person, via telephone, and online (social media and email). These “categories of social connections” included immediate family, relatives, friends, acquaintances, health professionals, neighbors or people from the same community, childhood friends, school friends, work colleagues, and friends they meet or have met through shared interests or volunteering. For each networking type, we tabulated the number of categories of social connections made. For example, if a respondent indicated that they connected with relatives and friends via telephone, this was considered to constitute two connections. For the analysis, caregivers were divided into LBP or non-LBP group; the LBP status was determined through the diagnosis of a doctor according to the criteria of the 10<sup>th</sup> edition of the International Statistical Classification of Diseases and Related Health Problems (ICD-10). The ADL performance of the patients was assessed by a healthcare professional using the Barthel Index<sup>24</sup>. For the analysis, t-tests and chi-squared tests were performed to compare the personal characteristics of the two LBP groups. Mann-Whitney U tests were then used to examine the differences between the two groups in terms of networking methods in order to describe the relationship between LBP status and social networking. Additionally, Spearman’s correlation coefficients were calculated in order to explore any significant relationships between networking methods and HRQOL. Next, by focusing on each networking method found to significantly correlate with the HRQOL, t-tests were performed to identify the social-connection categories within these methods that could also relate to the HRQOL. Finally, multiple regression analysis was performed to identify the family caregiver parameters that could significantly predict the HRQOL, with the EQ-5D score as the dependent variable. In addition to the LBP status, the factors found to have significant relationships with the EQ-5D score in the social network analysis described above were set as explanatory variables. Correlation analysis was then performed to check for multicollinearity among the explanatory variables. Analyses were performed using IBM SPSS Statistics 23.0, with a statistical significance level of 5%.

### 3. RESULTS

The characteristics of the subjects are shown in Table 1. Notably, significant differences between the LBP and non-LBP groups were found in the Barthel Index and EQ-5D scores. The LBP prevalence rate was 51.4% (males: 52.6%, females: 47.4%), and the mean EQ-5D score of the subjects was  $0.882 \pm 0.298$ . In addition, no significant difference between the two groups was found for gender ( $p = 0.481$ ). Sixty (81.1%) caregivers were immediate family members of the patients and 14 (18.9%) were other relatives. However, no significant difference between the LBP status groups was found in this factor ( $p = 0.911$ ), nor was there any significant difference in the EQ-5D scores ( $p = 0.945$ ).

Table 2 shows, for the two groups, the number of categories of social connections made through each networking method. A significant difference was found between the LBP status groups with regard to the number of categories of social connections made online, with the LBP group making more connections.

Table 3 shows, for LBP status, the correlations between the number of connection categories made through each networking method and the EQ-5D scores. For the LBP group, a significantly positive correlation was found between making connections in person and the EQ-5D scores.

Table 1. The characteristics of subjects in terms of LBP status

	LBP (N=38)	Non-LBP (N=36)
Age (yrs.)	45.1 ± 9.4	47.5 ± 9.8
Height (cm)	168.0 ± 8.2	165.9 ± 8.4
Weight (kg)	66.9 ± 18.3	65.4 ± 14.4
Duration of care (months)	5.4 ± 6.9	72.5 ± 235.2
Care time per day (min.)	821.6 ± 502.9	805.0 ± 487.7
Patient Barthel Index	40.1 ± 28.4	60.7 ± 29.3**
EQ-5D	0.822 ± 0.1	0.948 ± 0.1**

Values indicated are means ± SD. Unpaired t-test demonstrated the significant (\*\*p<0.01) group difference of “Patient Barthel Index” and “EQ-5D”.  
LBP=Low back pain

Table 2. Relationship between LBP status and the number of categories of social connections made using each networking method

Networking method	LBP (N=38)	Non-LBP (N=36)
In person	1.4 ± 0.8	1.5 ± 0.8
Telephone	2.5 ± 1.2	2.0 ± 1.0
Online	1.8 ± 1.5	1.1 ± 1.4*

Values indicated are the mean ± SD for the number of categories of social connections made (e.g., family + friends = 2). Unpaired t-test demonstrated the significant (\*p<0.05) group difference of “Online”.  
LBP=Low back pain

Table 3. Correlations between networking method and HRQOL by LBP status

Networking method	LBP (N=38)	Non-LBP (N=36)
In person	0.409*	0.024
Telephone	- 0.225	- 0.272
Online	0.079	- 0.082

Values indicated are Spearman’s correlation coefficients. \* p <0.05  
LBP=Low back pain

Table 4. Relationship between meeting in person/not meeting in person with social connections and EQ-5D scores in terms of LBP status

Variable	LBP Group (N=38)		Non-LBP Group (N=36)	
	Met in person	Did not meet in person	Met in person	Did not meet in person
Neighbors/members of the same community	0.854 ± 0.133	0.771 ± 0.101*	0.943 ± 0.097	0.979 ± 0.068
Friends from school	0.840 ± 0.121	0.813 ± 0.131	0.957 ± 0.096	0.954 ± 0.091
Work colleagues	0.842 ± 0.137	0.808 ± 0.122	0.963 ± 0.087	0.949 ± 0.093
Friends with shared interests	0.868 ± 0.121	0.815 ± 0.128	0.973 ± 0.076	0.948 ± 0.076
Friends from volunteer activities	-	0.822 ± 0.127	1.000	0.951 ± 0.092**

Values indicated are the mean ± SD for the EQ-5D scores. There are significant differences between "Met in person" and "Did not meet in person" in "Neighbors/members of the same community" and in "Friends from volunteer activities". \*p<0.05 \*\*p<0.01

The terms "Met in person" and "Did not meet in person" indicate whether or not the subjects met directly in person (i.e., "face-to-face") with each group of persons as specified in the Variable column. (Note that subjects could have had social connections with the Variable group already mentioned that were not "in person" (e.g., via email, via social networking, etc.).)

No caregivers with LBP indicated that they met with fellow volunteers in person, and the SD for non-LBP caregivers who met with fellow volunteers in person was 0. The social-connection category "childhood friends" was omitted here, as no participants indicated that they made that type of connection in person. LBP=Low back pain

Table 5. Multiple regression analyses of EQ-5D scores and relative caregivers' parameters

	B	β	t-value	95%CI	
Constant	0.799	0.000	8.653	0.614	0.983
LBP	-0.120	-0.467	-4.412	-0.174	-0.066
Number of social-connection categories met in person	0.033	0.213	1.827	-0.003	0.068
Having connections with neighbors/members of the same community	0.014	0.051	0.441	-0.048	0.075
Having connections with fellow volunteers	0.056	0.072	0.668	-0.111	0.223

The dependent variable was the EQ-5D score.

Adjusted R<sup>2</sup> = 0.275 \*\*p < 0.01 Covariates: age, gender

B: partial regression coefficient; β: standardized partial regression coefficient

LBP=Low back pain

Table 4 shows the EQ-5D scores for each in-person social-connection category in terms of the two LBP-status groups. Here, the EQ-5D score was found to be significantly higher in the LBP group in terms of networking in person with neighbors and people from the same community. For the non-LBP group, the EQ-5D was significantly higher in terms of networking in person with friends from volunteer activities.

Table 5 shows the results of the multiple regression analysis performed using the family caregiver parameters that had been found to significantly relate to the EQ-5D as explanatory variables and the EQ-5D score as the response variable. Specifically, the explanatory variables were: LBP status, the number of social-connection categories met in person, having connections with neighbors or members of the same community, and having connections with fellow volunteers. Of these factors, only LBP was found to significantly predict family caregiver EQ-5D score.

#### 4. DISCUSSION

According to Williams et al., the LBP prevalence rate for people over 50 years in China is 22%<sup>18)</sup>. The prevalence rate of 51.4% for the subjects of family caregivers in this study is significantly higher than this figure. This comparison is relevant because the mean age of the subjects (46.2 years) was close to 50 years. This finding supports that of Theilmeier et al., which suggests that caregivers have a higher risk of developing LBP than the average rate<sup>1)</sup>. The high prevalence rate in our subjects might have been due to family caregivers providing care for long periods of time, which has previously been found to cause physical and mental strain<sup>2),3)</sup>, leading to chronification and delays in recovery. Although we also asked in the questionnaire whether the subjects had LBP prior to providing patient care, most subjects did not respond. Minematsu reported that LBP occurred in 66.9% of employed caregivers after they started working, with 75.1% stating that LBP started during their first year of employment<sup>2)</sup>. Therefore, it is highly possible that LBP occurred in the subjects after they started providing care. With chronification, however, the subjects might not have been able to recall just when their LBP started. This point requires further investigation in a future longitudinal study.

The fact that the Barthel Index scores of the LBP group were lower (indicating less patient independence) than those of the non-LBP group suggests that caregivers with low scores may have a higher risk of developing LBP. In a study of nursing aides working at nursing homes for the elderly, Fujimura et al. found that LBP was related to the amount of assistance with ADL required by patients<sup>2)</sup>. Although the subjects in the present study were family caregivers, our results support this finding.

The EQ-5D scores of the LBP group were lower than those of the non-LBP group. As LBP has been shown to affect walking, ADL, and mental health<sup>7)</sup>, this finding suggests that lower EQ-5D scores may have been caused by LBP. The caregivers with LBP made online connections with more social categories of people than did those in the non-LBP group. According to Yamashita et al., family caregivers experiencing pain may, in an attempt to mitigate their pain, build social connections with relatives they can trust<sup>14)</sup>. In this study, the family members with LBP reported spending an average of 821.6 minutes (approximately 14 hours) per day with their patients. Given that most of the day was spent caring for the patient, it would naturally have been difficult for them to meet other people in person. Moreover, while some may have wanted to meet people in person, many caregivers may have decided to connect with them online because their LBP made it difficult for them to go out. However, no significant relationship was found between connecting with people online and the EQ-5D scores. This absence of a relationship between connecting with people online and HRQOL, as opposed to networking with people in person, might be due to the fact that non-verbal communication becomes very difficult, if not impossible, online<sup>25)</sup>. Reports have stated that depression, anxiety, etc.<sup>18), 19)</sup>, inhibit DLPFC activity, with a decline of analgesic effect for LBP<sup>11), 12)</sup>. The findings of this study suggest that meeting others face-to-face might reduce anxiety, with the possibility that DLPFC is activated with a significant alleviation of LBP.

Conversely, a significantly positive correlation between networking with people in person and the EQ-5D score was found for family caregivers with LBP. This suggests that for this group, meeting in person

rather than online is related to higher HRQOL. In their study of community-dwelling elderly individuals in China, Lei et al. reported that the subjects who rarely met with neighbors, relatives, or friends had lower HRQOL<sup>18)</sup>. While the subjects of this study differed, our finding that HRQOL may be improve when subjects meet others in person supports the finding of Lei et al.<sup>20)</sup> Further, our findings also suggest that in particular, meeting with neighbors or members of the same community in person may help maintain or improve the HRQOL.

Moreover, the results also showed that for family caregivers without LBP, EQ-5D scores were higher when they met in person with friends from volunteer activities. As it is unlikely that LBP had any impact on the physical activities of this group, it would have been possible for them to meet fellow volunteers who may have had a positive effect on their scores. Furthermore, the scores may also have been high given that participation in volunteer activities increases life satisfaction<sup>26)</sup>.

A multiple regression analysis was performed on the factors found to be significantly related to EQ-5D scores in these analyses: LBP status, the number of social-connection categories met in person, having connections with neighbors or members of the same community, and having connections with fellow volunteers. The results demonstrated that compared to social networking-related factors, the factor having the greatest effect on the HRQOL was whether the subjects had LBP. Therefore, the study suggests that for maintaining and improving the HRQOL, LBP is a more important factor than psychological factors related to social networking.

In LBP research conducted prior to the spread of the Internet and social media, a significant relationship was found between decline in social networks and the incidence of LBP<sup>13)</sup>. However, since the spread of the Internet, it has become possible for people suffering from LBP to connect with others online. Nevertheless, our analysis showed that online connection may not necessarily contribute to improvement in the HRQOL.

A limitation of this study was its small subject size. To verify these results, further studies on this topic using a larger subject from multiple Chinese hospitals are required.

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