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<Original Article>

Relationship between migraine and somatosensory amplification : a cross-sectional study

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Abstract : *Objective* : Although some evidence suggests that cognitive behavioral therapy is an effective psychosomatic treatment for migraine, few studies have examined cognitive distortion in patients with migraine. Therefore, in the present study, we examined difficulty with activities of daily living and somatosensory amplification in patients with migraine.

Methods : The present study included 29 patients with migraine (seven men, 22 women ; mean age : 43.4 ± 13.4 years) and 60 healthy control participants (six men, 54 women ; mean age : 24.0 ± 8.0 years). All participants were asked to complete the Somatosensory Amplification Scale (SSAS), Pain Catastrophizing Scale (PCS), Headache Impact Test-6 (HIT-6), and both the anxiety and depression components of the Hospital Anxiety and Depression Scale (HADS-A and HADS-D). After comparing responses between the groups, we examined the relationship between SSAS scores and headache symptoms/the degree of difficulty during daily life in patients with migraine.

Results : The migraine group exhibited significantly higher scores on the SSAS, PCS, HIT-6, and HADS than healthy individuals. Among patients with migraine, SSAS scores were positively correlated with total PCS scores and PCS magnification scores. HIT-6 scores exhibited a significant positive correlation with PCS helplessness scores, HADS-A scores, and headache severity. Covariance structure analysis revealed that SSAS exerted a significant impact on PCS scores, which in turn exerted a significant impact on HIT-6 scores.

Conclusion : Our findings demonstrated that somatosensory amplification was more severe in patients with migraine than in healthy controls. Furthermore, pain catastrophizing was directly associated with the degree of difficulty during daily life, while somatosensory amplification was indirectly associated with such difficulty via pain catastrophizing, among patients with migraine.

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Keywords : Allodynia, Cognitive behavioral therapy, Migraine, Pain catastrophizing, Somatosensory amplification

Introduction

Intractable migraines are often associated with psychosomatic complications such as psychosocial stress, anxiety, and depression, necessitating specialized assessment and intervention^{1)~3)}. Previous studies have indicated that cognitive behavioral therapy (CBT) is effective in the treatment of migraine, possibly via the treatment of cognitive distortions specific to the disorder⁴⁾⁵⁾. However, few studies have examined the effects of CBT on cognitive distortion in patients with migraine.

Migraine is a typical psychosomatic disorder of the nervous system, and several methods have been developed for the assessment of cognitive distortion in patients with psychosomatic disease, including somatosensory amplification⁶⁾.

According to Barsky et al., somatosensory amplification refers to the tendency to perceive ordinary physical stimuli as intense, noxious, and/or harmful. Patients exhibiting somatosensory amplification may selectively focus their attention on specific physical sensations, which then causes them to feel discomfort and concern regarding the pathological nature of the stimuli, regardless of their frequency or intensity. The self-rated Somatosensory Amplification Scale (SSAS) has been translated into several languages, and several studies have examined the association between SSAS scores and physical/psychiatric disorders. Indeed, SSAS scores exhibit significant associations with hypochondriasis⁷⁾, somatoform disorder⁸⁾, functional dyspepsia⁹⁾, irritable bowel syndrome¹⁰⁾, non-cardiac chest pain¹¹⁾, somatic symptoms in upper respiratory tract infections¹²⁾, health anxiety in patients with implantable cardioverter-defibrilla-

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tors¹³, perceived work stress in women¹⁴, psychoneurosis¹⁵, social anxiety disorder¹⁶, and subjective side effects associated with medical treatment¹⁷.

Only one Turkish study, published by Yavuz et al. in 2013, has examined the relationship between headache and somatosensory amplification¹⁸. In this previous study, the authors distributed the SSAS, Migraine Disability Assessment Scale (MIDAS), and Depression Anxiety Stress Scale (DASS) to 55 patients with migraine and 28 healthy controls. SASS scores were significantly higher in patients with migraine than in healthy individuals and tended to increase along with the severity of headache. In addition, a significant positive correlation was observed between MIDAS A scores (headache onset frequency in the past 3 months) and SASS scores.

Therefore, in the present study, we examined difficulty with activities of daily living and somatosensory amplification in patients with migraine to expand upon the findings of Yavuz et al.¹⁸. We hypothesized that SSAS scores would be higher in patients with migraine than in healthy participants, and that SSAS scores would correlate with the degree of difficulty during daily life in patients with migraine.

Methods

In the present cross-sectional study, we compared baseline characteristics and questionnaire responses between patients with migraine and healthy control participants. We then examined the relationship between SSAS scores and the degree of difficulty with activities of daily living in the migraine group. The migraine group was then divided into two groups based on gender, presence/absence of aura, allodynia, and relevant family history.

Participant characteristics

The migraine group included patients with migraine who had visited the psychosomatic medicine department of a university hospital in Tokyo and a neurosurgical hospital in Kanagawa prefecture. Diagnoses of migraine were made by a headache specialist in accordance with criteria outlined in the International Classification of Headache Disorders 3rd edition beta version (ICHD-3 β)¹⁹. Infants and patients with mental retardation, schizophrenia, or dementia were excluded from analysis under the assumption that they would be unable to respond appropriately to questions regarding headache and psychological symptoms. Healthy control participants were recruited from among individuals at a university and technical college in Tokyo. Based on headache questionnaire responses, those who may have met the diagnostic criteria for primary and secondary headache based on the ICHD-3 β were excluded from analysis.

Responses were obtained from 38 patients with migraine and 109 healthy individuals between February 25, 2015,

Table 1 The Somatosensory Amplification Scale (SSAS)⁷

- | |
|--|
| 1. When someone else coughs, it makes me cough too. |
| 2. I can't stand smoke, smog, or pollutants in the air. |
| 3. I am often aware of various things happening within my body. |
| 4. When I bruise myself, it stays noticeable for a long time. |
| 5. Sudden loud noises really bother me. |
| 6. I can sometimes hear my pulse or my heartbeat throbbing in my ear. |
| 7. I hate to be too hot or too cold. |
| 8. I am quick to sense the hunger contractions in my stomach. |
| 9. Even something minor, like an insect bite or a splinter, really bothers me. |
| 10. I have a low tolerance for pain. |

and March 16, 2016. Following the exclusion of ineligible participants and those who had provided inappropriate responses, we included 29 and 60 participants in the migraine and control groups, respectively.

Measures

All participants were asked to complete the SSAS, Pain Catastrophizing Scale (PCS), Headache Impact Test-6 (HIT-6), and both the anxiety and depression components of the Hospital Anxiety and Depression Scale (HADS-A and HADS-D).

The SSAS (Table 1) is a self-administered questionnaire consisting of 10 items regarding general body sensations, including respiratory, circulatory, and digestive organs as well as those involving the nervous system. Total scores are calculated based on responses provided along a five-point scale, with minimum and maximum scores of 10 and 50 points, respectively. Higher scores are considered indicative of more severe somatosensory amplification. The credibility and validity of the Japanese version of the SSAS have been demonstrated in a previous study²⁰.

The PCS is a self-administered questionnaire consisting of 13 items regarding one's thoughts and emotions during the experience of pain. Sub-items are used to evaluate rumination, helplessness, and magnification²¹. Total scores are calculated based on responses provided along a five-point scale, with minimum and maximum scores of 0 and 52, respectively. Higher scores are considered indicative of more intense pain catastrophizing. The credibility and validity of the Japanese version of the PCS have been demonstrated in a previous study²².

The HIT-6 is a self-administered questionnaire consisting of six items that is widely utilized to assess the degree of difficulty during daily life due to chronic headache. Total scores are calculated based on responses provided along a five-point scale (6, 8, 10, 11, or 13 points), with minimum and maximum scores of 36 and 78 points, respectively. Higher scores are considered indicative of greater difficulty in daily life due to chronic headache. Although originally developed by Quality Metric and Glaxo Wellcome (currently Glaxo SmithKline), the credibility and validity of the Japanese

Table 2 Comparison of scores between migraine and control groups

Characteristic	Migraine group (n = 29)	Control group (n = 60)	p
SSAS	32.0 ± 4.7	29.1 ± 5.8	0.03
PCS	26.5 ± 10.7	14.8 ± 10.3	<0.01
PCS (rumination)	13.6 ± 3.5	8.9 ± 5.3	<0.01
PCS (helplessness)	8.3 ± 5.4	3.7 ± 3.7	<0.01
PCS (magnification)	4.6 ± 3.1	2.1 ± 2.4	<0.01
HIT-6	62.9 ± 6.9	44.0 ± 6.7	<0.01
HADS-D	6.0 ± 3.9	3.8 ± 3.3	0.01
HADS-A	7.7 ± 3.4	5.2 ± 2.8	<0.01

n = number of participants, SSAS = Somatosensory Amplification Scale, PCS = Pain Catastrophizing Scale, HIT-6 = Headache Impact Test, HADS = Hospital Anxiety and Depression Scale (-D: depression, -A: anxiety)

version of the HIT-6 by Sakai et al. have been demonstrated in a previous study²³.

The HADS is a self-administered questionnaire consisting of 14 items designed to assess anxiety and depression in patients reporting physical symptoms²⁴. Zero to three points are assigned to responses provided along a four-point scale. Anxiety and depression are assessed using seven items each, with minimum and maximum scores of 0 and 21 points for each domain, respectively. Previous studies have demonstrated that the HADS, which has been translated into Japanese by Kitamura et al., is excellent for assessing anxiety and depression in patients with coexisting psychological and physical symptoms²⁵. Its credibility and validity have been demonstrated when assessing anxiety and depression in patients with primary headache disorders²⁶.

Statistical analysis

IBM SPSS Statistics version 19 and Amos 6.0 were used for all statistical analyses. Qualitative data are presented as the number/percentage of samples. Quantitative data are presented as the mean value and standard deviation. Median values were compared using Mann-Whitney U tests. Spearman's rank correlation coefficients were used to assess correlations between scale scores. Multiple regression analysis was used to predict the causal correlation between factors. The level of statistical significance was set at $p < 0.05$, while p values < 0.10 were considered to indicate marginal significance.

Ethics approval and consent to participate

The present study was approved by the Ethics Committee of Toho University School of Medicine (No. 27034, 26077). All participants provided written informed consent prior to completing the questionnaire package. The questionnaire was consolidated, anonymous, and self-completed, and included the statement that all responses were entirely voluntary.

Results

The migraine group included seven men and 22 women with a mean age of 43.4 years (SD = 13.4), whereas the con-

Table 3 Clinical characteristics of migraineurs

	Migraineurs (n = 29)	
	n	%
Headache severity		
Mild	1	3.4
Moderate	21	72.4
Severe	7	24.1
Frequency of headaches (per month)		
7 days or less	10	34.5
8 days or more, and 14 days or less	12	41.4
15 days or more	7	24.1
Aura		
With aura	18	62.1
Without aura	11	37.9
Accompanying symptoms		
Nausea and vomiting	21	72.4
Photophobia	19	65.5
Phonophobia	19	65.5
Lacrimation	3	10.3
Nasal obstruction	3	10.3
Nasal discharge	4	13.8
Ear fullness	5	17.2
Allodynia		
With allodynia	8	27.6
Without allodynia	21	72.4
Family history		
With family history	23	79.3
Without family history	6	20.7

n = number of participants

trol group included six men and 54 women with a mean age of 24.0 years (SD = 8.0). Table 2 shows the mean values and standard deviations of each assessment scale in the migraine and control groups. The migraine group exhibited significantly higher scores on all sub-items of the SSAS, PCS, HIT-6, and HADS than the control group. After adjustment for age, the migraine group exhibited significantly higher scores on all sub-items of the SSAS, PCS, and HIT-6 than the control group.

Table 3 shows clinical characteristics of migraineurs. Table 4 shows the correlation coefficients between each assessment scale in the migraine group. SSAS scores exhibited a marginally significant positive correlation with total

Table 4 Spearman's rank correlation coefficients between scores in the migraine group

Migraineurs (n = 29)											
	SSAS	PCS	PCS (rumination)	PCS (helplessness)	PCS (magnification)	HIT-6	HAD-D	HAD-A	Headache severity	Headache frequency	Age
SSAS		0.31 [†]	0.30	0.23	0.37*	0.03	0.22	0.27	0.24	0.11	0.14
PCS			0.79**	0.86**	0.81**	0.29	0.24	0.28	0.13	0.40*	0.23
PCS (rumination)				0.56**	0.72**	0.04	0.22	0.26	0.14	0.20	0.31
PCS (helplessness)					0.52**	0.45*	0.29	0.38*	0.29	0.56**	0.15
PCS (magnification)						0.16	0.19	0.20	-0.01	0.24	0.15
HIT-6							0.25	0.42*	0.58**	0.29	-0.14
HADS-D								0.57**	0.31	0.33 [†]	0.16
HADS-A									0.29	0.59**	0.17
Headache severity										0.15	-0.03
Headache frequency											0.22
Age											

n = number of participants, SSAS = Somatosensory Amplification Scale, PCS = Pain Catastrophizing Scale, HIT-6 = Headache Impact Test, HADS = Hospital Anxiety and Depression Scale (-D: depression, -A: anxiety)

[†] p < 0.10, * p < 0.05, ** p < 0.01

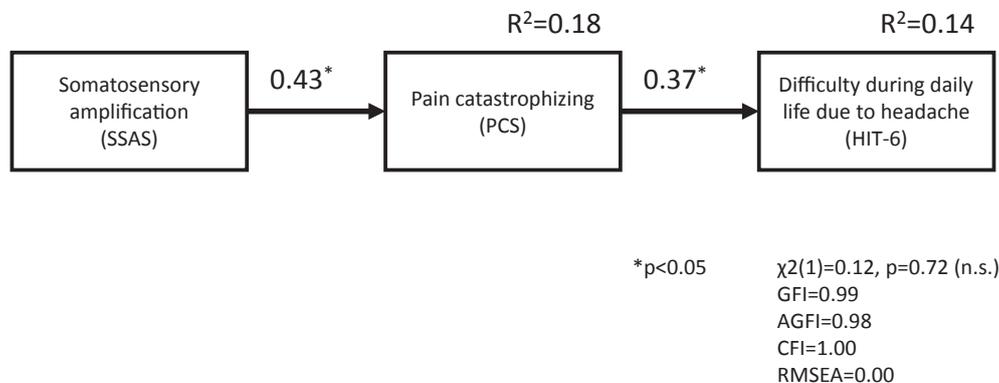


Figure 1 Results of covariance structure analysis for SSAS, PCS, and HIT-6 scores in migraineurs. SSAS scores significantly influenced PCS scores, and PCS scores significantly influenced HIT-6 scores. SSAS: Somatosensory Amplification Scale; PCS: Pain Catastrophizing Scale; HIT-6: Headache Impact Test-6.

PCS scores, and a significant positive correlation with PCS magnification scores. PCS scores were also significantly positively correlated with headache frequency. HIT-6 scores exhibited a significant positive correlation with PCS helplessness scores, HADS-A scores, and headache severity. Total PCS scores were significantly positively correlated with scores for each sub-item.

Casual correlations between cognitive distortion and the degree of difficulty in daily life in patients with migraine were examined via multiple regression analysis using the forced entry method. When HIT-6 was used as the dependent variable and each sub-item of the SSAS, PCS, and HADS was used as an independent variable, we observed a significant positive effect of PCS helplessness scores ($\beta = 0.67, p = 0.01$).

Covariate structure analysis was performed to examine multiple models of the relationship among SSAS, PCS, and HIT-6 scores. Figure 1 shows the model adopted for the migraine group. The path coefficient indicates the standard-

ized estimate. The indices of model assessment were as follows: $\chi^2(1) = 0.12$ ($p = 0.72$), GFI = 0.99, AGFI = 0.98, CFI = 1.00, and RMSEA = 0.00. In the control group, each path coefficient from SSAS to PCS and from PCS to HIT-6 was non-significant.

We then examined differences in mean values for all sub-items of the SSAS, PCS, HIT-6, and HADS in the migraine sub-groups. Men ($n = 7$) (31.0 ± 3.8) exhibited lower mean scores on the SSAS than women ($n = 22$) (32.3 ± 4.9), although no significant differences were observed for any item. HADS-A scores were significantly higher in patients with aura ($n = 18$) than in those without aura ($n = 11$) (8.9 ± 3.3 vs. 5.9 ± 2.6 ; $p = 0.01$). Patients with allodynia ($n = 8$) exhibited significantly higher SSAS scores than those without allodynia ($n = 21$) (36.1 ± 5.4 vs. 30.4 ± 3.4 ; $p < 0.01$). No significant differences in any items were observed between patients with a relevant family history ($n = 23$) and patients without a family history ($n = 6$).

Discussion

In the present study, we examined difficulty with activities of daily living and somatosensory amplification in patients with migraine, who exhibited significantly higher scores on the SSAS, PCS, HIT-6, and HADS than healthy controls. These findings are in accordance with those reported by Yavuz et al¹⁸⁾. Among patients of the migraine group, women exhibited higher mean SSAS scores than men. The proportion of women was higher in the control group than in the migraine group, and previous studies have also reported that women exhibit higher SSAS scores than men¹³⁾¹⁴⁾¹⁶⁾. Higher SSAS scores in the migraine group may have been caused by essential differences in the characteristics of migraine onset.

In the migraine group, SSAS scores exhibited a marginally significant correlation with PCS scores, while PCS scores also exhibited a significant correlation with headache frequency. Yavuz et al. also reported a significant correlation between SSAS scores and headache frequency. Taken together, these findings indicate that headache frequency among patients with migraine is correlated with cognitive distortion in a broad sense as assessed by the SSAS and PCS. However, cognitive distortions regarding the intensity of the headache may have affected the frequency of analgesic use. Thus, further studies are required to determine the relationship between somatosensory amplification and medication overuse headaches.

In accordance with the findings of Yavuz et al., depression and anxiety scores as assessed using the HADS were significantly higher in the migraine group than in the control group¹⁸⁾. Although numerous epidemiological studies have examined the hypothesis that migraine is associated with psychological symptoms such as depression and anxiety, as well as the potential role of serotonin in this association, no definitive relationship has been identified. In the current study, we observed a marginally significant correlation between HADS-D scores and headache frequency, as well as a significant correlation between HADS-A scores and headache frequency in the migraine group. These findings indicate that treatment of complications such as depression, anxiety may aid in reducing headache frequency in patients with migraine. However, further studies are required to examine the efficacy of these therapeutic interventions.

Our multiple regression analyses suggested that PCS helplessness scores exerted a significant impact on the degree of difficulty during daily life due to headache, as measured using the HIT-6. Although somatosensory amplification did not seem to affect HIT-6 based on our multiple regression analysis, it may have exerted an indirect impact on the degree of difficulty during daily life due to its signifi-

cant correlation with PCS scores. Covariance structure analysis indicated that SSAS scores significantly influenced PCS scores, and that PCS scores significantly influenced HIT-6 scores, in the migraine group. These results suggest that pain catastrophizing is directly associated with the degree of difficulty during daily life, and that somatosensory amplification is indirectly associated with such difficulty via pain catastrophizing. These results are relatively consistent with a previously reported model for patients with somatoform disorder²⁷⁾. We speculated that the degree of difficulty during daily life due to headache is enhanced by pain catastrophizing associated with somatosensory amplification.

Among patients of the migraine group, those with allodynia (36.1 ± 5.4) exhibited significantly higher SSAS scores than those without allodynia (30.4 ± 3.4). Although many of the neurophysiological mechanisms underlying somatosensory amplification remain unclear, previous studies have suggested that somatosensory amplification is associated with the P300 amplitude of event related potentials (ERP)²⁸⁾. In addition, functional MRI studies have revealed that a neural circuit framework consisting of the anterior cingulate cortex, insula, amygdala, hippocampal formation, and striatum may be involved in somatosensory amplification²⁹⁾. Since allodynia is associated with central nervous system sensitization in the trigeminal spinal nuclei and thalamus, somatosensory amplification and allodynia may share a common underlying neurophysiological mechanism.

Our results suggest that the SSAS can be used to assess cognitive distortion in patients with migraine, and that such assessments can be performed in conjunction with the PCS. Indeed, previous studies have reported that CBT can reduce PCS scores³⁰⁾. Our findings support the notion the CBT targeting somatosensory amplification may represent a novel treatment strategy for cognitive distortion in patients with migraine.

Limitations

In the current study, we utilized self-administered questionnaires for the assessment of psychological symptoms such as depression and anxiety. Therefore, future studies should combine such assessments with more objective methods in order to verify our findings. In addition, we observed a statistically significant difference in age between the migraine and control groups, as participants in the latter group were recruited from among healthy university students. However, SSAS, PCS, and HIT-6 scores were not affected by age adjustment, and no significant associations between SSAS and age were observed in the present or previous studies. Therefore, we judged that these scores were appropriate for our analyses. In addition, SSAS values in the control group were higher than those reported in previous studies, which may have been caused by the higher proportion of women in the control group.

Thus, further studies involving age- and gender-matched groups are required in order to more accurately identify SSAS characteristics specific to migraine.

Conclusions

Our findings demonstrated that somatosensory amplification was more severe in patients with migraine than in healthy controls. Furthermore, somatosensory amplification exhibited a marginally significant positive correlation with pain catastrophizing among patients with migraine. Our findings suggested that somatosensory amplification exerts an indirect effect on the degree of difficulty during daily life due headache among patients with migraine via pain catastrophizing. These findings further indicate that the SSAS can be used to identify cognitive distortion in patients with migraine.

The author state that they have no Conflicts of Interest (COI)

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片頭痛と身体感覚増幅傾向についての検討

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³⁾間中病院

片頭痛における認知の歪みを評価するため Somatosensory amplification scale (SSAS), Pain catastrophizing scale (PCS), Headache impact test (HIT-6) を用いた調査を行った。片頭痛群 29 名, 健常者群 60 名が検討対象となった。片頭痛群では健常者群と比較して SSAS, PCS, HIT-6 の全てが有意に高値を示した。共分散構造分析による検討では SSAS は PCS を介して HIT-6 に間接的な影響を及ぼしているというモデルが採択された。SSAS は片頭痛における認知の歪みを把握するために有用であることが示唆された。

Key words : 片頭痛, 身体感覚増幅傾向, 痛みに対する破局的思考, 認知行動療法, アロディニア