している[23、24]ことから支持される。その一方で、慢性疼痛患者はADLやQOLが改善したことを医療者同様に高く評価し満足する者もいれば、仮にADLとQOLが障害されたままであったとしても痛み自体が緩和することだけを望む者もいる。また、患者の家族の多くは、ADLやQOLが改善したことに対して満足することは多い。したがって、慢性疼痛の診療では、痛みに関わる立場が異なれば目標が大きく異なる。このことをもう少し巨視的に観察すると、慢性疼痛患者の雇用主は患者の痛みが緩和しようがしまいがADLが改善し復職した場合には、その後の疼痛診療のために休職する可能性や痛みによる労働生産性の低下、収益減について思案するかもしれない。さらに巨視的には、健康保険者や行政の立場としては、慢性疼痛患者が現在と将来的に要する医療費の総額が評価の対象となるかもしれない。このように慢性疼痛の医療では、よりミクロな環境として医師-患者の視点からマクロな環境として行政、保険システムという観点で、必要な医療と社会保障を考えなければならない[25]。本邦は国民皆保険が整備されているため、国民全員がstakeholder（利害関係者）の一員であると捉えれば、これは国民全体の問題である。痛みが慢性化している患者のすべてに、現在の医療で想定されるすべての治療法を適応するという考えは、膨大な医療費によって国家自体が立ち行かなくなり、国民が均等に医療を受けられなくなり結果的に慢性疼痛患者にとって不利益となる。このような患者の不利益を生み出さないためにも、社会的サポートに上限を設定することが長期的視点では患者利益に繋がる可能性が考えられる。今後、このような社会的ニーズについても医療と司法、行政が議論を重ねていく機会がもたれることが望まれる。

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ORIGINAL ARTICLE

The Japanese version of the modified ACR Preliminary Diagnostic Criteria for Fibromyalgia and the Fibromyalgia Symptom Scale: reliability and validity

Chie Usui · Kotaro Hatta · Satoko Aratani · Naoko Yagishita · Kenya Nishioka · Teruhisa Kanazawa · Kenji Itoh · Yoshihisa Yamano · Hiroyuki Nakamura · Toshihiro Nakajima · Kusuki Nishioka

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Abstract
Purpose The aim of this study is to investigate the reliability and validity of the Japanese version of the modified American College of Rheumatology (ACR) Preliminary Diagnostic Criteria for Fibromyalgia (mACR 2010-J) and the Fibromyalgia Symptom Scale (mFS-J).
Methods According to the ACR 1990 classification criteria, patients with chronic pain were divided into the fibromyalgia group and nonfibromyalgia group (rheumatoid arthritis and osteoarthritis). Patients in both groups were assessed using mACR 2010-J and mFS-J.
Results 294 of 462 (64 %) patients in the fibromyalgia group met mACR 2010-J, whereas 4 % (9/231) of the nonfibromyalgia group did, with sensitivity of 64 %, specificity of 96 %, positive predictive value of 97 %, negative predictive value of 56 %, and positive likelihood ratio of 16.3. Mean total scores on mFS-J significantly differentiated the fibromyalgia from the nonfibromyalgia group. According to the value of the Youden index, the best cutoff score for the mFS-J was 9/10.
Conclusion Our findings indicate that mACR 2010-J as a positive test and mFS-J as a quantification scale might be suitable for assessing fibromyalgia among Japanese chronic pain populations.

Keywords Diagnostic criteria · Fibromyalgia · Symptom scale · Modified ACR Preliminary Diagnostic Criteria for Fibromyalgia

Introduction

Fibromyalgia (FM) is characterized by widespread musculoskeletal chronic pain, fatigue, poor sleep, frequent psychological difficulties, and multiple tender points on physical examination [1, 2]. In 1990, the American College

C. Usui (✉) · K. Hatta
Department of Psychiatry, Juntendo University Nerima Hospital, 3-1-10 Takanodai, Nerima-ku, Tokyo 177-8521, Japan
e-mail: chiec@juntendo.ac.jp

S. Aratani · T. Nakajima · K. Nishioka
Institute of Innovative Medical Science and Education, Tokyo Medical University, 6-1-1 Shinjuku, Shinjuku-ku, Tokyo 160-8402, Japan

N. Yagishita · Y. Yamano
Institute of Medical Science, St. Marianna University School of Medicine, 2-16-1 Sugo, Miyamae-ku, Kawasaki, Kanagawa 216-8511, Japan

K. Nishioka
Department of Neurology, Juntendo University School of Medicine, 2-1-1 Hongo, Bunkyo-ku, Tokyo 113-8421, Japan

T. Kanazawa
Department of Rheumatology, Tokyo Medical University Ibaraki Medical Center, 3-20-1 Chuo, Ami-cho, Inashiki-gun, Ibaraki 300-0395, Japan

K. Itoh
Department of Rheumatology, National Center for Global Health and Medicine, 1-21-1 Toyama, Shinjuku-ku, Tokyo 162-8655, Japan

H. Nakamura
Department of Environmental and Preventive Medicine, Graduate School of Medical Science, Kanazawa University, Kakuma-cho, Kanazawa, Ishikawa 920-1192, Japan

of Rheumatology (ACR) presented FM criteria (ACR 1990) that required tenderness on pressure (tender points) in at least 11 of 18 specified sites and the presence of widespread pain for diagnosis [1]. Widespread pain was defined as axial pain, both left- and right-sided and with upper and lower segment pain. However, ACR 1990 had the serious problem of little variation in symptoms. To improve this shortcoming, new clinical criteria, which integrate variations in symptoms with severity scale (2010 ACR Preliminary Diagnostic Criteria for FM, ACR 2010) [3], have been presented. The diagnostic criteria for FM are satisfied if the following three conditions are met: (1) Widespread Pain Index (WPI) $\geq$7 and Symptom Severity Score (SS) $\geq$5, or WPI of 3–6 and SS $\geq$9; (2) symptoms have been present at a similar level for at least 3 months; and (3) the patient does not have a disorder that would otherwise explain the pain. The publication of ACR 2010 eliminated the tender point examination, thus making it possible to study FM in survey and clinical research.

Accordingly, we have validated the Japanese version of ACR 2010 [4]. In addition, we have originally validated the Japanese version of the Fibromyalgia Symptom Scale with the sum of WPI and the original SS, i.e., fatigue, waking unrefreshed, cognitive symptoms, and somatic symptoms in general consisting of 41 symptoms of the FS-J [4]. Both ACR 2010-J and FS-J have high reliability and validity, and are useful for assessing fibromyalgia among Japanese chronic pain populations.

Recently, Wolfe et al. [5] proposed a modification of the ACR 2010 (mACR 2010), deleting 38 out of 41 somatic symptoms in general from the original SS. Consequently, complete self-administration has become possible. Furthermore, they created the Fibromyalgia Symptom Scale with the sum of WPI and the new SS (FS). They reported that the criteria properly identified diagnostic groups, and that FS score $\geq$13 best separated criteria+ and criteria− patients.

The aim of this study is to investigate the reliability and validity of the Japanese version of the mACR 2010 (mACR 2010-J) and the Japanese version of the FS (mFS-J). Furthermore, our questions are whether mACR 2010-J would be more useful than ACR 2010-J for assessing fibromyalgia among Japanese chronic pain populations, and whether mFS-J is more suitable than FS-J as a positive test.

Subjects and methods

An experienced rheumatologist and an experienced psychiatrist had translated the mACR 2010 into Japanese with the author's permission and produced forward- and back-translations to create the mACR 2010-J.

We recruited FM patients who met the previous criteria of the ACR 1990 and were without psychiatric disorders according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) [6] in a clinic specialized for FM, the Kasumigaseki Urban Clinic, in Tokyo, Japan, between August 1, 2010 and July 31, 2011. During the study period, other patients with diseases associated with chronic pain such as rheumatoid arthritis (RA) and osteoarthritis (OA) who had not been diagnosed previously with FM were recruited as control patients. To adjust the imbalance of number of patients, control patients were additionally recruited from May 30 to July 2, 2012. The diagnoses of RA and OA were made according to the 2010 rheumatoid arthritis classification criteria [7] and the American College of Rheumatology criteria for classification and reporting of osteoarthritis of the hand, hip, and knee [8–10]. The experienced rheumatologist and the experienced psychiatrist familiar with FM assessed these patients. This study was approved by the Institutional Review Board of Kasumigaseki Urban Clinic.

After obtaining informed consent from study participants, the rheumatologist rated patients with the mACR 2010-J. In order to assess interrater reliability, another rater independently rated a subset of the same subjects ($N = 19$) while blind to the diagnoses and scores of the other rater. The raters in this study were already fully trained in use of the scale and quite experienced in use of it. We therefore decided that only a small subsample was needed to reevaluate consistency across raters.

Statistics

Data were analyzed using SPSS 17.0-J software. Differences among groups in demographic and clinical characteristics were calculated with the unpaired t test. If data were not sampled from Gaussian distributions, a nonparametric test (Mann–Whitney U test) was used. To compare categorical data, we used Fisher's exact test.

In the present study, the control group was not healthy volunteer but consisted of chronic pain patients with RA and OA. It has been reported that the age-specific incidence of RA peaked in the 60–64 and 70–74 year age groups for females and males, respectively, in Taiwan [11]. Similarly, it has been reported that the peak prevalence of knee OA in women and men was $\geq$80 years in Japan [12]. In contrast, we have reported that the frequent age of onset of FM in women was 35–55 years based on our FM database including 3,500 Japanese patients with FM [13]. Among Asians, thus, patients with FM are much younger than those with RA and OA. Therefore, matching age of control patients with age of FM patients seems to be rather arbitrary. Accordingly, to control for the effect of age on the rate of patients meeting the mACR 2010-J, patients were divided into three age categories, i.e., 20–39, 40–59, and $\geq$60 years.

There were only eight FM patients and one non-FM patients less than 20 years of age, and there were only two FM patients and three non-FM patients 80 years or older. Then, the Mantel–Haenszel method was used to test the difference in the percentage of patients meeting the mACR 2010-J between the two groups. Also, to control for the effect of age on the score on the mFM-J, one-way analysis of covariance was used. The internal consistency for the mFM-J was calculated with Cronbach's α. Interrater reliability was measured with the intraclass correlation coefficient (ICC) for pairs of independent raters. Cutoff scores for the mFS-J were determined using receiver-operator characteristic (ROC) analyses to determine the Youden index when comparing the FM group with all non-FM subjects. Positive predictive value (PPV), negative predictive value (NPV), and positive likelihood ratio (sensitivity/1 − specificity) were also calculated. All statistical tests were two-tailed. Statistical significance was set at $p < 0.05$.

Results

A total of 462 patients meeting the ACR 1990 (the FM group) and a total of 231 non-FM patients (RA patients, 196; OA patients, 35; the non-FM group) were enrolled. Demographic and clinical characteristics of the groups are presented in Table 1, showing that 294 of 462 (64 %) patients in the FM group met the mACR 2010-J, whereas 4 % (9/231) of the non-FM group did, including 4 % (8/196) of RA patients and 3 % (1/35) of OA patients. The percentage of patients meeting the mACR 2010-J criteria in the FM group was significantly higher than that of the non-FM group after adjusting for age (estimated odds ratio, 35.7, $p < 0.0001$; Table 1). The sensitivity, specificity, PPV, NPV, and positive likelihood ratio for comparison of the FM group with all non-FM subjects were 64, 96, 97, 56, and 16.3 %, respectively. The ICC between the two independent raters was very high for the mACR 2010-J, at 0.877.

The mean score (standard deviation, SD) of mFS-J in the FM group was 16.7 (6.5), while that in the non-FM group was 3.7 (4.1). The mean score of mFS-J in the FM group was significantly higher than that of the non-FM group after adjusting for age ($F = 605.1$, $p < 0.0001$; Table 1). Internal consistency was not high, with a Cronbach's α coefficient for the mFS-J (WPI + the modified SS) of 0.603. ROC analyses were performed for the mFS-J, comparing the FM group with the non-FM group. Table 2

Table 1 Demographic and clinical characteristics of the fibromyalgia group and nonfibromyalgia group

Group	Fibromyalgia ($N = 462$)	Nonfibromyalgia ($N = 231$)		p
		RA ($N = 196$)	OA ($N = 35$)	
Mean age (SD), years	50.6 (14.8)	61.3 (13.9)		<0.0001
		60.6 (14.4)	65.5 (10.2)	
Sex (female), N (%)	389 (84)	188 (81)		0.39
		160 (82)	28 (80)	
Patients meeting the mACR 2010-J,[a] N (%)	294 (64)	9 (4)		<0.0001[c]
		8 (4)	1 (3)	
Mean score (SD) of mFS-J[b]	16.7 (6.5)	3.7 (4.1)		<0.0001[d]
		3.7 (4.2)	3.9 (3.3)	

[a] The Japanese version of the modified 2010 ACR Preliminary Diagnostic Criteria for Fibromyalgia

[b] The Japanese version of the Fibromyalgia Symptom Scale (WPI + modified SS)

[c] To control for the effect of age on the rate of patients meeting the mACR 2010-J, patients were divided into three age categories. Then, the Mantel–Haenszel method was used to test the difference in the percentage of patients meeting the mACR 2010-J between the two groups

[d] To control for the effect of age on the score of the mFM-J, one-way analysis of covariance was used

SD standard deviation

Table 2 Sensitivity and specificity of the Japanese version of the Fibromyalgia Symptom Scale (mFS-J), based on receiver-operating characteristics (ROC) analysis: fibromyalgia group versus nonfibromyalgia (RA and OA) group

Cutoff score	Sensitivity (%)	Specificity (%)	Positive likelihood ratio	Youden index
8.5	87.7	89.2	8.1	0.769
9.5	84.8	92.2	10.9	0.770
10.5	82.0	92.2	10.5	0.742

shows the sensitivity, specificity, positive likelihood ratio, and Youden index for ROC analysis at various cutoff scores for the mFS-J. According to the value of the Youden index, the best cutoff score for the mFS-J was 9/10.

Discussion

This is the first study to validate the mACR 2010-J and mFS-J, which is the quantification scale of the mACR 2010-J. The positive likelihood ratio of 16.3 for the mACR 2010-J is sufficiently high as a positive test. We cannot directly compare the likelihood ratios for the mACR 2010-J and the ACR 2010-J, as the present study group is quite different from that used in the study of the ACR 2010-J [4]. However, the value of mACR 2010-J is sufficiently high compared with that of ACR 2010-J, for which the positive likelihood ratio was 8.8. Therefore, the modification of ACR 2010-J may be superior to the original ACR 2010-J as a positive test.

The best cutoff score for the mFS-J was 10, which is just the same as the FS-J [4]. Furthermore, the positive likelihood ratio for the mFS-J (Table 2) is as high as that for the FS-J at the cutoff score [4]. As the mFS-J is simpler than the FS-J, mFS-J may be superior to FS-J based on the original ACR 2010-J as a quantification scale. Meanwhile, the best cutoff score of 10 in the present study is smaller than that of the original study on the FS performed in the USA (cutoff score 13) [5]. One explanation for this difference is in patient characteristics. In the present study, comorbid psychiatric disorders were excluded, while in the previous study they were not. Patients with major depressive disorder, panic disorder, or anxiety disorder usually have somatic symptoms similar to those of ACR 2010, and comorbidity of major depressive disorder, panic disorder, or anxiety disorder is not rare [1]. Therefore, the population in the previous study may have been modified by comorbid psychiatric disorders. Thus, the cutoff score of 10 in the present study might reflect fibromyalgia itself more than that of 13 in the previous study. Another possible explanation is cross-cultural differences in expression or rating of symptoms.

The internal consistency with a Cronbach's α coefficient for the mFS-J (WPI + the modified SS) of 0.603 is lower than that for the FS-J (WPI + the original SS) of 0.747 [4]. The modified SS consists of fatigue, waking unrefreshed, cognitive symptoms, plus having pain/cramps in the abdomen, depression, and headache, resulting from 38 somatic symptoms in general having been deleted from the original SS. Therefore, the modified SS values neuropsychiatric symptoms more than the original SS. In contrast, WPI is the number of pain areas, which is simply somatic. Accordingly, the internal consistency for the mFS-J (WPI + the modified SS) might have been lower than that for the FS-J (WPI + the original SS). As FM shows a variety of symptoms and is suspected of involving not only musculoskeletal but also central nervous system [14], the not so high value of internal consistency for the mFS-J may not necessarily be a shortcoming.

Thus, mACR 2010-J as a positive test and mFS-J as a quantification scale might be suitable for assessing fibromyalgia among Japanese chronic pain populations. A strength of the present study is that the findings represent real clinical practice in Japan, since the study was performed in a clinic specialized in FM which is visited by the largest number of FM patients in Japan. A limitation of this study is that the findings may not be applicable to all patients, since FM patients with other musculoskeletal diseases, such as spondylitis, were not included in it. Further studies with patients of other countries or ethnicities will be needed to determine cross-cultural or ethnic differences in expression or rating of symptoms.

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Conflict of interest None.

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RESEARCH ARTICLE Open Access

Vulnerability to traumatic stress in fibromyalgia patients: 19 month follow-up after the great East Japan disaster

Chie Usui[1*], Kotaro Hatta[1], Satoko Aratani[2], Naoko Yagishita[3], Kenya Nishioka[4], Satoko Okamura[5], Kenji Itoh[6], Yoshihisa Yamano[3], Hiroyuki Nakamura[7], Nozomu Asukai[8], Toshihiro Nakajima[2] and Kusuki Nishioka[2]

Abstract

Introduction: The aim of this study was to investigate vulnerability and long-term influence of traumatic stress caused by the Great East Japan Disaster which occurred on March 11, 2011, in patients with fibromyalgia, which is a chronic pain syndrome probably involving central sensitization.

Methods: A total of 60 female patients with fibromyalgia were compared with female patients with rheumatoid arthritis (RA, n = 23) as another chronic pain disease, and with female healthy controls (HC, n = 26) in the observational study. To evaluate responses to traumatic stress, the scores of Impact of Event Scale-Revised (IES-R) were assessed one month after the disaster and every six months until 19 months after the disaster. We also evaluated levels of depression during the study period. To know the score of IES-R of patients with fibromyalgia during usual living, we assessed IES-R in another population of fibromyalgia patients without exposure to a great disaster.

Results: The mean score of IES-R one month after the disaster in the fibromyalgia group (24.6 [SD 18.9]) was significantly higher than that of RA group (13.4 [SD 14.5]) or HC group (9.1 [9.2]) ($F = 9.96$, $p < 0.0001$). However, the mean score of IES-R in fibromyalgia patients without exposure to a great disaster was (20.3 [SD 18.7]), which was almost the same value as the fibromyalgia group seven months after the disaster (20.2 [SD 19.5]). Repeated measures analysis of variance showed significant effect of time course in the depression-related symptoms ($F = 6.68$, $P = 0.001$), and a post-hoc test revealed that the number of depression-related symptoms one month before the disaster was significantly different from other time points until 19 months after the disaster, respectively.

Conclusions: Although response to acute stress induced by the great earthquake was likely to be settled within seven months after the disaster, depression-related symptoms have been increasing for more than one year after the disaster, despite exclusion of patients with major depression at baseline. This long-lasting worsening of depression-related symptoms may have been in response to chronic stress induced by the fear of radiation due to the nuclear power disaster. These findings suggest that patients with fibromyalgia are vulnerable to chronic stress rather than acute stress.

Introduction

On 11 March 2011, a magnitude 9.0 earthquake struck the east coast of Japan. The total number of people who died in the earthquake and the subsequent tsunami is approximately 19,000. To make the situation worse, the Fukushima nuclear power plants were seriously damaged and it took 9 months to settle the subsequent nuclear reactor problems. The earthquake registered 5 to 6 on the Japan Meteorological Agency seismic intensity scale in Tokyo areas, which caused acute stress to people who lived in Tokyo. The nuclear power disaster caused continuous stress not only to people in the disaster-stricken areas but also to people in Tokyo areas due to records above the normal range of radiation during 1 month after the disaster (Tokyo Metropolitan Institute of Public Health). The response to such acute and subacute traumatic stress should therefore have been monitored even in Tokyo, especially in patients with diseases involving psychological factors.

Fibromyalgia is characterized by widespread musculoskeletal chronic pain, fatigue, poor sleep, frequent psychological

* Correspondence: chiec@juntendo.ac.jp
[1]Department of Psychiatry, Juntendo University Nerima Hospital, 3-1-10 Takanodai, Nerima-Ku, Tokyo 177-8521, Japan
Full list of author information is available at the end of the article

difficulties, and multiple tender points on physical examination [1,2]. The etiology of fibromyalgia is unknown but may involve neuropsychiatric vulnerability [3]. There is evidence of the relationship between traumatic experiences and prevalence of fibromyalgia diagnosis [4,5], but a long-term follow-up study does not exist. Meanwhile, effects of traumatic stress induced by the World Trade Center terrorist attacks on pain have not been detected between before and after 11 September 2001 [5].

The aim of this study was to investigate vulnerability and long-term influence to traumatic stress caused by the Great East Japan Disaster in patients with fibromyalgia, compared with patients with rheumatoid arthritis (RA) as another chronic pain disease and with healthy controls. In addition, change in the severity of fibromyalgia between before and after the disaster was also examined.

Methods

We recruited fibromyalgia patients who had been followed up before the earthquake in a clinic specialized for fibromyalgia, the Kasumigaseki Urban Clinic, in Tokyo, Japan, between 11 April and 18 April 2011. Fibromyalgia was diagnosed according to the previous criteria for the 1990 classification of the American College of Rheumatology [1]. Patients concomitant with psychiatric disorders according to the Diagnostic and Statistical Manual of Mental Disorders – IV [6] were excluded. Also, patients whose prescription had been changed at their visit to the clinic just before the disaster were excluded. During the study period, RA patients who had been followed up before the disaster were also recruited to represent another musculoskeletal chronic pain disease. The diagnosis of RA was made according to the 2010 RA classification criteria [7]. Healthy subjects from hospital workers were also enrolled as controls. All subjects in the present study neither received direct physical harm nor were exposed to harmful level of radiation. Also they did not lose their family member lives. This study was approved by the Institutional Review Board of Kasumigaseki Urban Clinic. Written informed consent was obtained from all participants.

To evaluate responses to traumatic stress, scores on the Impact of Event Scale – Revised (IES-R) were assessed 1 month after the disaster and every 6 months until 19 months after the disaster in the three groups: fibromyalgia patients, RA patients, and healthy controls. The IES-R is a 22-item self-rating scale to evaluate traumatic stress symptoms developed by Weiss [8]. The scale consists of three subscales: Intrusion, Avoidance, and Hyperarousal. The Japanese-language version of the IES-R has been well validated [9].

The severity of fibromyalgia was assessed using the Fibromyalgia Symptom Scale (mFS-J [10]). The mFS-J consists of the Widespread Pain Index (WPI) and the Symptom Severity scale. The WPI represents the number of areas in which the patient has had pain over the last week. The rater examines whether patients have pain or not in 19 areas of their body. The score will be between 0 and 19. The Symptom Severity scale is the sum of the severity of the three symptoms (fatigue, waking unrefreshed, cognitive symptoms) plus the extent (severity) of somatic symptoms in general. The final score is between 0 and 12. At the clinic, fibromyalgia patients had been assessed by the first and last authors using the mFS-J at every visit before the disaster. The intra-class correlation coefficient between the two independent raters was very high for the mFS-J, at 0.994 [10]. Pre-disaster scores of the mFS-J in the present study were based on the assessment records within 1 month before the disaster. The mFS-J was then assessed by the first author 1 month after the disaster and every 6 months until 19 months after the disaster.

Similarly, the severity of RA after the disaster was compared with that before the disaster according to inflammation data of RA, such as C-reactive protein, white blood cell counts, and the erythrocyte sedimentation rate. The pre-disaster data had been collected within 1 month before the disaster.

To evaluate levels of depression during the study period, we identified five depression-related symptoms common to mFS-J and a major depressive episode of the Diagnostic and Statistical Manual of Mental Disorders – IV (that is, fatigue/tiredness, thinking of or remembering problems, insomnia, depression, and loss of appetite), and analyzed the time course of the total number of these symptoms present.

To determine the IES-R score for fibromyalgia patients during usual living, we recruited age-matched patients with fibromyalgia who were outpatients of Daiichi Hospital located in Kochi-City, in the western part of Japan, in June 2013. Inclusion criteria were being female and without exposure to a great disaster. At the same time, we assessed the IES-R for fibromyalgia patients in Tokyo we followed up.

Statistical analysis

Data were analyzed using SPSS 20-J software (IBM Japan, Tokyo, Japan). Differences among groups in demographic and clinical characteristics were calculated with one-way analysis of variance (ANOVA) and the *post-hoc* Tukey–Kramer multiple comparisons test was used. If data were not sampled from Gaussian distributions, a nonparametric test (Mann–Whitney *U* test) was used. To compare categorical data, we used Fisher's exact test. To examine changes in the score for mFS-J or depression-related symptoms, repeated-measures ANOVA was used. We compared the IES-R scores in subjects among fibromyalgia, RA patients, and controls after correcting for age, using one-way analysis of covariance (ANCOVA) with age as

covariate. For multiple comparisons, the Bonferroni test was used. Linear correlation between IES-R scores and mFS-J and its subscale scores was examined. All statistical tests were two-tailed. Statistical significance was set at P <0.05.

Results

Baseline characteristics

A total of 80 female patients with fibromyalgia, 32 female patients with RA, and 30 female healthy controls were enrolled, and 60 (75%), 23 (72%), and 26 (87%) subjects completed the follow-up period, respectively. Other patients dropped out due to a change of clinics, and four healthy controls dropped out due to a change of jobs. Demographic and clinical characteristics of the groups are presented in Table 1.

Change in main symptoms in patients with fibromyalgia and patients with RA before and after the disaster

The change in mFS-J is shown in Figure 1. Repeated-measures ANOVA revealed no significant effect of time course (F = 1.80, P = 0.13). We also analyzed the time course of the WPI, a score that represents only pain and accounts for 61% (19/31) of the mFS-J, resulting in no significant effect of time course (F = 1.30, P = 0.28). Similarly, in patients with RA there was no significant change in the mean levels of C-reactive protein, white blood cell counts, and erythrocyte sedimentation rate. Patients with fibromyalgia received the following medication before the disaster: pregabalin, 53 patients; gabapentin, 24 patients; and duloxetine, 12 patients. Patients with RA received the following medication before the disaster: methotrexate, 14 patients; TNFα inhibitors, 13 patients; IL-6 inhibitor, four patients; T-cell activation inhibitor, three patients; and prednisolone, 18 patients. Additional medications including an increase in dose within 6 months after the disaster were 31 for the fibromyalgia group (duloxetine, six patients; benzodiazepines, six patients; gabapentin, five patients; pregabalin, four patients; nonsteroidal anti-inflammatory drugs, four patients; lamotrigine, three patients; quetiapine, three patients) and eight for the RA group (pregabalin, three patients; TNFα inhibitors, two patients; gabapentin, one patient; benzodiazepines, one patient; lamotrigine, one patient). There was no significant difference in the rate between the groups (52% vs. 35%, P = 0.22), suggesting only minimal effects of additional medication after the disaster on the present results.

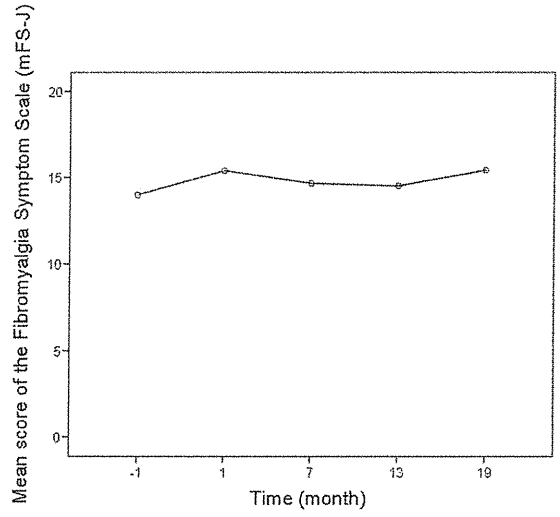

Figure 1 Change in the score of the Fibromyalgia Symptom Scale. Repeated-measures analysis of variance revealed no significant effect of time course (F = 1.80, P = 0.13). mFS-J, Fibromyalgia Symptom Scale.

Development of stress-related symptoms in patients with fibromyalgia, patients with RA, and healthy controls after the disaster

ANCOVA showed that there was significant difference in the mean IES-R score 1 month after the disaster among the three groups after adjusting for age (F = 9.96, P <0.0001). The Bonferroni *post-hoc* multiple comparisons test showed that the mean IES-R score 1 month after the disaster in the fibromyalgia group (24.6 (standard deviation (SD) 18.9)) was significantly higher than that of the RA group

Table 1 Baseline characteristics of patients

	Healthy control (*N*= 26)	Rheumatoid arthritis (*N* = 23)	Fibromyalgia (*N* = 60)	*P* value
Age (years)[a]	42.3 (12.5)	56.0 (14.4)	48.4 (14.8)	0.0047
Asian	26/26 (100)	23/23 (100)	60/60 (100)	
Duration of illness (years)		7.4 (6.7)	6.4 (7.4)	0.31
Living alone[b]	5/26 (19)	3/23 (13)	6/60 (10)	0.32
Unemployed[b]	0/26 (0)	3/23 (13)	9/60 (15)	0.066
Comorbid disease		14/23 (61)	39/60 (65)	0.80

Data represent mean (standard deviation) or *n/N* (%), unless otherwise indicated. [a]Tukey–Kramer multiple comparisons test showed that mean age in the rheumatoid arthritis group was higher than that in the healthy control group (P <0.01). [b]Healthy control group versus others.

(13.4 (14.5)) (P = 0.036) or the healthy control group (9.1 (9.2)) (P <0.0001). Repeated-measures ANCOVA revealed significant main effects of time course (F(3,315) = 3.32, P = 0.030) and group (F(2,105) = 11.5, P <0.0001) on change in the IES-R score (Figure 2). However, there was no significant interaction between time course and group on change in the IES-R score (F(6,315) = 0.20, P = 0.96). Similar results were observed in all of three subscales of the IES-R: Intrusion, Avoidance, and Hyperarousal (Figure 3).

There were significant correlations not only between IES-R and mFS-J (r = 0.52, P <0.0001), but also between IES-R and WPI (r = 0.40, P = 0.0016) 1 month after the disaster. Also, there were significant correlations at all other following periods between IES-R/mFS-J and IES-R/WPI: r = 0.50, P <0.0001 and r = 0.40, P = 0.0017, respectively, for 7 months after the disaster; r = 0.51, P <0.0001 and r = 0.43, P = 0.0006, respectively, for 13 months after the disaster; and r = 0.51, P <0.0001 and r = 0.43, P = 0.0007, respectively, for 19 months after the disaster. Moderate correlations between the IES-R score and the mFS-J score and between the IES-R score and the WPI score were thus found at time points after the disaster, and fluctuations in the correlations were very small.

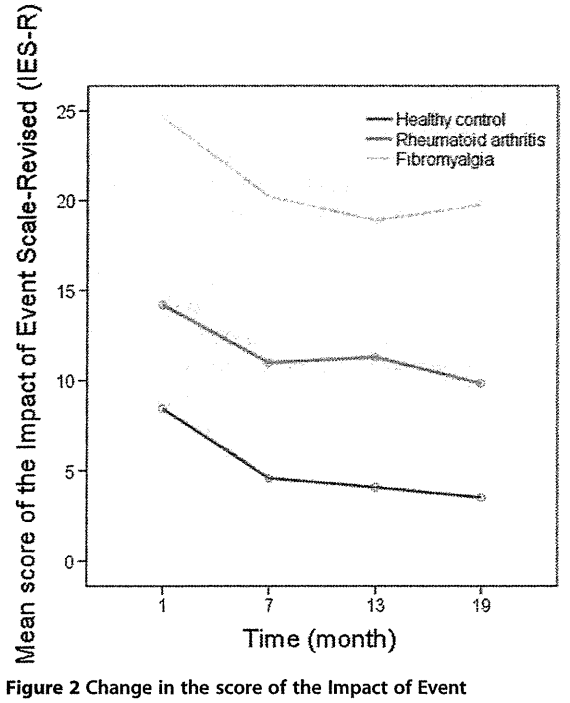

Figure 2 Change in the score of the Impact of Event Scale – Revised. Repeated-measures analysis of covariance revealed significant main effects of time course (F(3,315) = 3.32, P = 0.030) and group (F(2,105) = 11.5, P <0.0001) on change in the Impact of Event Scale – Revised (IES-R) score. However, there was no significant interaction between time course and group on change in the IES-R score (F(6,315) = 0.20, P = 0.96).

Estimation of the IES-R score in patients with fibromyalgia during usual living

Twenty age-matched patients with fibromyalgia in Kochi were included as another population of fibromyalgia patients without exposure to a great disaster. Meanwhile, among 60 patients with fibromyalgia in Tokyo we followed up, we could assess the IES-R in 58 patients at the same time. The mean age of fibromyalgia patients in Kochi was 50.6 years (SD 12.7), which was similar to the mean age of the fibromyalgia group in Tokyo (50.5, SD 14.3, t = 0.024, P = 0.98). The mean IES-R score of the fibromyalgia patients in Kochi in June 2013 was 20.3 (SD 18.7), and that of the fibromyalgia patients in Tokyo at the same time was 18.6 (SD 19.4). There was no significant difference in the mean IES-R score between the fibromyalgia patients in Kochi and the fibromyalgia patients in Tokyo (t = 0.33, P = 0.74), suggesting that the IES-R score of fibromyalgia patients during usual living is approximately 20. Furthermore, the mean IES-R score in fibromyalgia patients without exposure to a great disaster (20.3, SD 18.7) was almost the same value as the fibromyalgia group 7 months after the disaster (20.2, SD 19.5).

These findings strongly suggest that the mean IES-R score 7 months after the disaster in the fibromyalgia group had already returned to baseline. Change in the mean IES-R score between 1 month and 7 months after the disaster was therefore compared between the groups. ANCOVA showed that there was no significant difference in the mean change in score on IES-R among the three groups after adjusting for age (3.8 for healthy controls, 3.2 for RA, 4.4 for fibromyalgia at the age of 48.6; F = 0.072, P = 0.93). The amplitude of acute response to the event in fibromyalgia patients may thus not necessarily be greater than that of another population.

Depression-related symptoms in patients with fibromyalgia before and after the disaster

Repeated-measures ANOVA showed a significant effect of time course in the depression-related symptoms (F = 6.68, P = 0.001) (Figure 4). The Bonferroni *post-hoc* multiple comparisons test revealed significant differences in the number of depression-related symptoms between 1 month before the disaster and 1 month after the disaster (P = 0.006), between 1 month before the disaster and 13 months after the disaster (P <0.0001), and between 1 month before the disaster and 19 months after the disaster (P = 0.010). There were no significant correlations between the number of depression-related symptoms and the score of IES-R at any time points (r = −0.030, P = 0.82 for 1 month after the disaster; r = 0.020, P = 0.88 for 7 months after the disaster; r = −0.067, P = 0.61 for 13 months after the disaster; and r = −0.096, P = 0.46 for 19 months after the disaster).

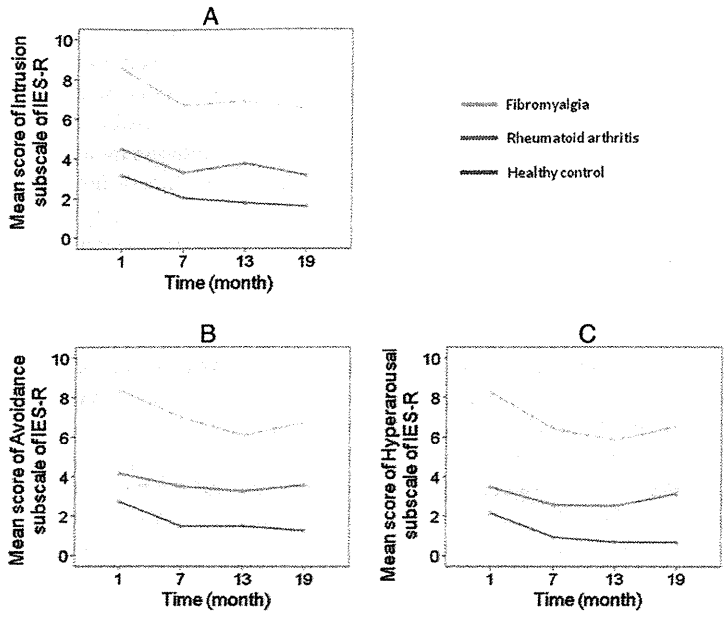

Figure 3 Change in the subscale scores of the Impact of Event Scale – Revised. (A) Intrusion: repeated-measures analysis of covariance (ANCOVA) revealed significant main effects of time course ($F(3,315) = 3.11$, $P = 0.027$) and group ($F(2,105) = 10.1$, $P < 0.0001$) on change in the Impact of Event Scale – Revised (IES-R) score. However, there was no significant interaction between time course and group on change in the IES-R score ($F(6,315) = 0.17$, $P = 0.99$). **(B)** Avoidance: repeated-measures ANCOVA revealed significant main effects of time course ($F(3,315) = 4.60$, $P = 0.004$) and group ($F(2,105) = 10.3$, $P < 0.0001$) on change in the IES-R score. However, there was no significant interaction between time course and group on change in the IES-R score ($F(6,315) = 0.28$, $P = 0.95$). **(C)** Hyperarousal: repeated-measures ANCOVA revealed main effects of time course as trend level ($F(3,315) = 2.39$, $P = 0.069$) and significant main effects of group ($F(2,105) = 19.2$, $P < 0.0001$) on change in the IES-R score. However, there was no significant interaction between time course and group on change in the IES-R score ($F(6,315) = 0.65$, $P = 0.69$).

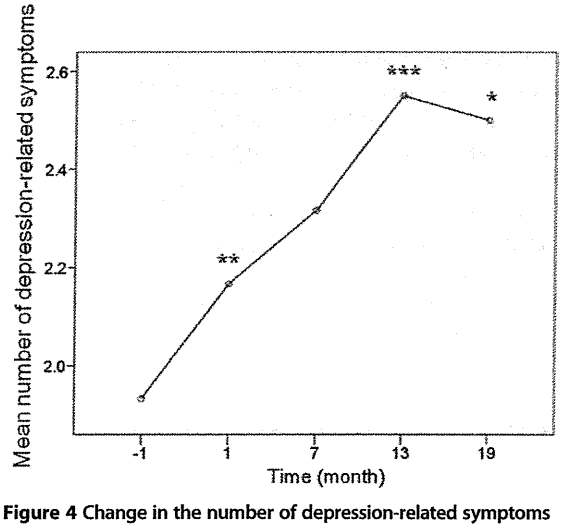

Figure 4 Change in the number of depression-related symptoms in the fibromyalgia group. Repeated-measures analysis of variance showed a significant effect of time course in the depression-related symptoms ($F = 6.68$, $P = 0.001$). The Bonferroni *post-hoc* multiple comparisons test revealed significant differences in the number of depression-related symptoms between 1 month before the disaster and 1 month after the disaster ($P = 0.006$)**, between 1 month before the disaster and 13 months after the disaster ($P < 0.0001$)***, and between 1 month before the disaster and 19 months after the disaster ($P = 0.010$)*.

Discussion

The present finding of an extremely high IES-R score in the fibromyalgia group 1 month after the disaster, compared with healthy controls or patients with RA as another chronic pain disease, is remarkable. The degree of the score is equivalent to patients with post-traumatic stress disorder (PTSD) [9]. However, the estimated IES-R score in patients with fibromyalgia during usual living was approximately 20. The cutoff value of screening for PTSD is 24/25 in the Japanese version of the IES-R [9], so the baseline value itself in patients with fibromyalgia is extremely high. This finding is consistent with the report on the prevalence of fibromyalgia and PTSD that suggests PTSD is a potential risk factor of fibromyalgia and *vice versa* [11], or with the high prevalence of fibromyalgia after traumatic stress experiences [4,5]. Malt and colleagues found a tendency to overreact to triggers in patients with fibromyalgia using the Eysenck Personality Questionnaire [12]. Lundberg and colleagues found independent personality patterns between fibromyalgia and normal controls triggered by the ability to cope with stress [13]. In fibromyalgia patients, increased harm avoidance and high persistence have been found using the Temperament and Character Inventory [9,11]. In addition, hyperarousal might be intrinsically

characteristic in fibromyalgia, considering the subscale score of the IES-R presented here. These characteristics might explain the high IES-R score in the fibromyalgia group.

As mentioned in Results, the mean IES-R score of 7 months after the disaster in the fibromyalgia group had probably already returned to baseline. Accordingly, stress-related symptoms may not have lasted for more than 7 months even in patients with fibromyalgia as well as in patients with RA or in healthy controls. The response to acute stress induced by the great earthquake was thus likely to be settled within 7 months after the disaster. Furthermore, there was no significant difference in change in mean IES-R scores between 1 month and 7 months after the disaster between the groups, suggesting that the amplitude of response to the traumatic event in patients with fibromyalgia may not necessarily be greater than that of other populations.

In contrast to stress-related symptoms, depression-related symptoms in patients with fibromyalgia have been increasing for more than 1 year after the disaster compared with the level before the disaster, despite exclusion of patients with major depression at baseline. This long-lasting worsening of depression-related symptoms may have been a response to chronic stress induced by the fear of radiation due to the nuclear power disaster. These findings suggest that patients with fibromyalgia are vulnerable to chronic stress rather than acute stress.

The disaster consisted of not only a natural disaster but also a manmade disaster; that is, the nuclear power plant accident. Manmade disaster is known to be a risk factor for PTSD [14], and is reported to be associated with high prevalence of fibromyalgia [15]. However, as Tokyo is far from the disaster-stricken areas and the nuclear power plants, all of the subjects in the present study neither received direct physical harm nor were exposed to adverse levels of radiation. Also they did not lose their family member lives. Therefore, whether the disaster was natural or manmade may not sufficiently have influenced the results. Nevertheless, repeated aftershocks of the earthquake and fear of exposure to radiation might have been continuous stress for a while rather than an acute stress. Such continuous stress might have influenced fibromyalgia patients.

In the present study, no significant change in the main symptoms of fibromyalgia represented by the mFS-J or significant change in pain symptoms represented by the WPI was observed. Nevertheless, significant correlations between IES-R and mFS-J and between IES-R and WPI were found. We should mention superficial mismatched results among no significant effects of the time course in the mFS-J, significant changes in the IES-R during the time course, and the linear correlation between IES-R and mFS-J scores or between IES-R and WPI scores. The correlation coefficients between IES-R and mFS-J scores and between IES-R and WPI scores were approximately 0.5 and 0.4, respectively, indicating moderate correlations. Although P values of the effect of time course in the mFS-J and WPI were 0.13 and 0.28, respectively, they might become statistically significant in larger samples. Moderate correlation could occasionally be detected in such a situation.

There have so far been two studies on the change in symptoms of fibromyalgia or fibromyalgia-like pain before and after the World Trade Center terrorist attacks on 11 September 2001. Raphael and colleagues reported in a large community sample of women that a cohort initially surveyed for pain and psychiatric symptoms before 11 September were recontacted approximately 6 months after the attacks to assess current symptoms and specific terrorism-related exposures. They concluded that the attacks did not relate to the fibromyalgia-like symptoms [15]. Williams and colleagues found that pain levels of eight fibromyalgia patients in Washington, DC on the day after the attack did not differ significantly from pain levels before the attack [5]. Our result that a significant change in the mFS-J, the severity of fibromyalgia, was not observed is consistent with the previous observations. However, Yunus and colleagues reported that pain severity was influenced by psychological factors in fibromyalgia patients [16]. The moderate but significant relationship between stress-related symptoms and pain in fibromyalgia patients presented here is a new finding, but may be conceptually included in the findings by Yunus and colleagues.

Recently, findings indicating an association between pathophysiology of fibromyalgia and central nervous system dysfunction, such as the default mode network regions [3] and amygdale [17,18], have been accumulating. In PTSD, evidence for disrupted equilibrium between salience and default mode brain networks has been reported [17], as well as dysfunction of amygdala [18]. The vulnerability to traumatic stress in fibromyalgia presented here thus implicates common neural circuitry.

The strengths of the present study are that this is the first describing long-term follow-up of a disease cohort after the disaster, and that the findings represent real clinical practice in Tokyo since the study was performed in a specialized clinic for fibromyalgia that is visited by the largest number of fibromyalgia patients in Japan. A limitation of this study is the imbalance of the number of subjects among groups because this observational study started just after the disaster.

Conclusions

Although the response to acute stress induced by the great earthquake was likely to be settled within 7 months after the disaster, as indicated by change in the IES-R score, depression-related symptoms have been increasing for

more than 1 year after the disaster despite exclusion of patients with major depression at baseline. This long-lasting worsening of depression-related symptoms may have been a response to chronic stress induced by the fear of radiation due to the nuclear power disaster. These findings suggest that patients with fibromyalgia are vulnerable to chronic stress rather than acute stress.

Abbreviations
ANCOVA: Analysis of covariance; ANOVA: Analysis of variance; IES-R: Impact of Event Scale – Revised; IL: Interleukin; mFS-J: Fibromyalgia symptom scale; PTSD: Post-traumatic stress disorder; RA: Rheumatoid arthritis; TNF: Tumor necrosis factor; WPI: Widespread pain index.

Competing interests
The authors declare that they have no competing interests.

Authors' contributions
CU conceived the hypothesis for the study, participated in data collection, conducted data management, wrote the first draft of the manuscript, and was primarily responsible for the process of manuscript writing. KH, NA and HN conducted statistical analyses and contributed to the study design, analysis and interpretation of data. SO, SA, NY, KN, NA, HN, YY, KI, KN, and TN participated in study design, analysis and interpretation of data. All authors critically reviewed, contributed to, and approved the final manuscript.

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Author details
[1]Department of Psychiatry, Juntendo University Nerima Hospital, 3-1-10 Takanodai, Nerima-Ku, Tokyo 177-8521, Japan. [2]Institute of Innovative Medical Science and Education, Tokyo Medical University, 6-1-1 Shinjyuku, Shinjyuku-ku, Tokyo 160-8402, Japan. [3]Institute of Medical Science, St. Marianna University School of Medicine, 2-16-1 Sugo, Kawasaki, Miyame-ku, Kanagawa 216-8511, Japan. [4]Department of Neurology, Juntendo University School of Medicine, 2-1-1 Hongo, Bunkyo-Ku, Tokyo 113-8421, Japan. [5]*Kochi-Daiichi Hospital, 2-14 Kutanda, Kochi 780-0832, Japan.* [6]*Department of* Rheumatology, National Center for Global Health and Medicine, 1-21-1Toyama, Shinjuku-ku, Tokyo 162-8655, Japan. [7]Department of Environmental and Preventive Medicine, Graduate School of Medical Science, Kanazawa University, Kakuma-cho, Kanazawa-city, Kanazawa 920-1192, Japan. [8]Department of Psychiatry and Behavioral Sciences, Tokyo Metropolitan Institute of Medical Science, 2-1-8 Kamikitazawa, Setagaya-ku, Tokyo 156-8506, Japan.

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原著論文

運動イメージによる疼痛抑制効果の検討*

城由起子[1)]，松原貴子[2)]，大場千尋[3)]
小川美有[3)]，石河直樹[3)]，中島裕貴[4)]

要旨
【目的】運動は疼痛のリハビリテーションプログラムのひとつとして推奨されているが，臨床において運動の実施は困難な場合が多い。一方，運動による疼痛制御には運動野の賦活が重要な因子であると考えられており，この運動野の賦活は実際の運動を伴わない運動イメージによっても生じることが知られている。一方，近年，心拍変動（HRV）は自律神経活動のみならず運動および疼痛関連脳領域活動を反映することが示されている。そこで本研究は運動イメージによる疼痛抑制効果についてHRVや運動に伴う末梢生理的変化とともに検討した。
【方法】対象は健常男性40名とし，自転車エルゴメータによる下肢駆動運動を行う運動群と運動イメージを行うイメージ群に分類し，それぞれ20分間行った。測定項目は，僧帽筋の圧痛耐性値（PPT），血液循環動態およびHRVとした。血液循環動態は近赤外分光装置を用い，総ヘモグロビン（⊿THb），酸素化ヘモグロビン（⊿O_2Hb）および脱酸素化ヘモグロビン（⊿HHb）の各濃度変化量を測定した。HRVは心拍数および心電図R-R間隔の周波数解析から低周波数成分（LF）と高周波数成分（HF）およびLF/HFを算出した。
【結果】PPTは両群とも介入により有意に上昇した。⊿THbと⊿O_2Hbおよび心拍数は，運動群で有意に上昇したのに対し，イメージ群は変化しなかった。また，HFは運動群のみ低下したのに対しLF/HFは両群とも有意に上昇した。
【結論】実際の運動のみならず運動イメージによっても広汎性に痛覚感受性は低下した。さらに，運動イメージでは実際の運動を伴わないため血液循環動態や心拍数の変化は認めなかったが，LF/HFは運動実施群と同様に亢進した。このことから，運動イメージは実運動と同様に運動関連脳部位を賦活した可能性が示唆され，運動野を含む何らかの中枢性疼痛修飾系を介した疼痛抑制効果をもたらすと考えられた。

キーワード　運動イメージ，疼痛抑制，自律神経活動

はじめに

近年，各国のガイドラインにおいて，運動は腰痛などの運動器疼痛に対するリハビリテーションのひとつとして広く推奨されている[1)]。また，歩行や自転車エルゴメータなどの有酸素運動は，骨格筋への血液供給量を増加し[2)]，さらに広汎性の疼痛抑制効果をもたらすことが報告されている[3)]。運動による疼痛抑制機序として，このような骨格筋への血液供給量の変化など末梢組織の生理的変化によるもののみでなく，一次運動野や補足運動野の活動による視床下部や前頭前野を介した下行性疼痛抑制系の作用，ノルアドレナリン分泌によるストレス鎮痛効果が考えられている[4)]。また，臨床においても経頭蓋磁気刺激や経頭蓋直流電気刺激を用い運動野を賦活させることによる鎮痛が図られている[5)]。しかし，このような運動は術後の安静や固定，痛みなどのために実施困難な場合が多く，また，運動野への物理刺激は臨床で簡便に行えるものではない。

一方，運動観察や運動イメージは実際の運動実行時と重複する脳領域の活動を惹起することが知られており，機能的磁気共鳴画像（functional magnetic resonance imaging: fMRI）やポジトロン断層法（positron emission tomography: PET）を用いた研究においても，運動イメージによる一次運動野や前頭前野，運動前野の賦活が確認されている[6,7)]。また，運動イメージは複合性局所疼痛症候群（complex regional pain syndrome: CRPS）や幻肢痛など慢性の難治性疼痛の治療としても用いられており，痛みの原因を感覚情報の不一致と捉え，末梢の当該局所（疼痛肢の対側や周辺部）をターゲットとした鏡やバーチャル画像を利用した運動イメージにより感覚情報を調整する

* Effect of motor image on pain sensitivity in healthy male volunteers

1) 名古屋学院大学リハビリテーション学部理学療法学科
2) 日本福祉大学健康科学部リハビリテーション学科
3) 名古屋学院大学人間健康学部リハビリテーション学科
4) 名古屋大学医学部付属病院

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ことによって痛みを軽減しようとする試みがおこなわれている[8]。

自律神経活動の指標として心拍変動（heart rate variability: HRV）は広く使用されている。HRVは心電図R-R間隔の周波数解析から，交感神経と副交感神経両方の活動指標である低周波数帯（low frequency: LF, 0.04-0.15 Hz），副交感神経の活動指標である高周波数帯（high frequency: HF, 0.15-0.4 Hz），交感神経活動を反映するとされるLF/HF比（LF/HF）が算出される[9,10]。健常者では運動により心拍数は上昇，HFは減少，LF/HFは上昇する[9,10]。さらに，近年，fMRIやPETを用いた研究において，HRVと前頭前野や前帯状回，扁桃体の活動との関係性が報告され，HRVが脳活動を反映することが示され始めている[11]。

しかしながら，運動イメージによる疼痛抑制効果について，HRVを含め生理学的に検証した報告や広汎性の疼痛制御機序について検討した報告は見受けられない。運動による疼痛抑制機序として運動関連脳領域の活動が重要な因子であるならば，運動時と同様の脳領域活動が惹起される運動イメージによっても疼痛抑制効果が広汎性に得られ，同時に末梢生理的反応が生じる可能性が考えられる。そこで，本研究では自転車エルゴメータによる下肢駆動運動とその運動イメージを行い，主運動部と離れた遠隔部の広汎な痛覚感受性変化と筋血液循環動態および自律神経活動の変化を比較し，運動イメージによる疼痛抑制効果について生理的に検討した。

方法

本研究は，名古屋学院大学医学研究倫理審査委員会の承認（番号：2012-011）を得て行った。対象は，健常男性40名（21.3±0.6歳）とし，実際に運動を行う運動群20名（21.4±0.5歳）と運動イメージのみを行うイメージ群20名（21.1±0.7歳）に無作為に振り分けた。なお，頚肩部および下肢に外傷や疼痛の既往があるもの，運動習慣があるものは除外した。また，すべての対象者に対し，実験1週間前より激しい運動を禁止した。運動群は，自転車エルゴメータによる下肢駆動運動を強度50W，回転速度60回転/分で20分間行った。イメージ群は，自転車駆動運動のイメージを20分間行った。イメージの方法は，運動群と同様の下肢駆動運動を他人が実際に行っている姿を座位にて観察しながら，あたかも自分が運動しているようなイメージを行うように指示し，5分毎にイメージへの注意・集中を口頭にて促した。なお，介入前後15分間を閉眼座位にて安静とした。測定項目は，右僧帽筋の圧痛耐性値（pressure pain tolerance: PPT）と筋血液循環動態ならびに自律神経活動の指標である心拍数およびHRVとした。PPTはデジタルプッシュプルゲージ(RX-20, AIKOH)を用い，介入前（pre），介入開始10分後（ex 10），介入終了直後（post 0）および終了15分後（post 15）に測定し，得られた値から介入前の値を基準とした変化率を算出し測定値とした。なお，測定はすべて同一検者が行った。血液循環動態は，近赤外分光装置（NIRO-200，浜松ホトニクス）を用い，酸素化ヘモグロビン（⊿O_2Hb），脱酸素化ヘモグロビン（⊿HHb）および総ヘモグロビン（⊿THb: ⊿O_2Hb+⊿HHb）の各濃度変化量を実験中経時的に測定した。HRVは携帯型心拍変動記録装置（AC-301A, GMS）を用いて心電図を実験中経時的に測定し，心拍数および心電図R-R間隔の周波数解析（Memcalc / Win: Suwa Trust）からHFとLF/HFを算出した。血液循環動態とHFおよびLF/HFはPPTと同期させた時点からそれぞれ前3分間の平均値を算出し，pre, ex 10, post 0, post 15の測定値とした。

統計学的解析は，経時的変化にはFriedman検定およびTukey-typeの多重比較検定，群間比較はMann-Whitney検定を用い，有意水準は全て5%未満とした。なお，各ヘモグロビン濃度変化量の群間比較はeffect sizeを算出しMann-Whitney検定を行った。

結果

PPTは，preと比べ運動群でpost 0，イメージ群でex 10とpost 0で有意な上昇を示し，群間では差を認めなかった（図1）。

⊿THbと⊿O_2Hbは，preと比べ運動群でpost 0で有意な上昇を示したのに対し，イメージ群は変化しなかった（図2A,B）。群間比較では，⊿THb

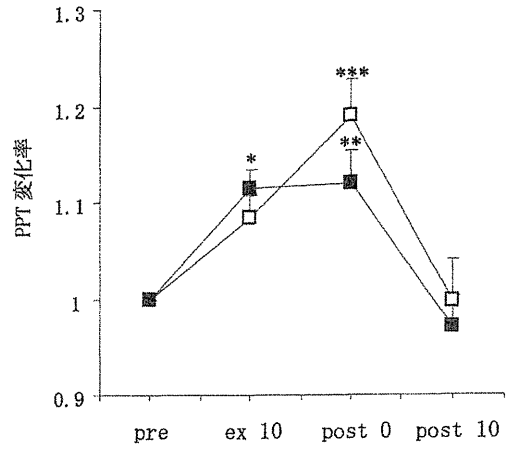

図1 運動または運動イメージによる僧帽筋圧痛耐性値（PPT）変化率の変化
□：運動群，■：イメージ群
PPT: pressure pain tolerance, 平均±SE.,
*, **, *** $p<0.05$, 0.01, 0.001 vs. pre

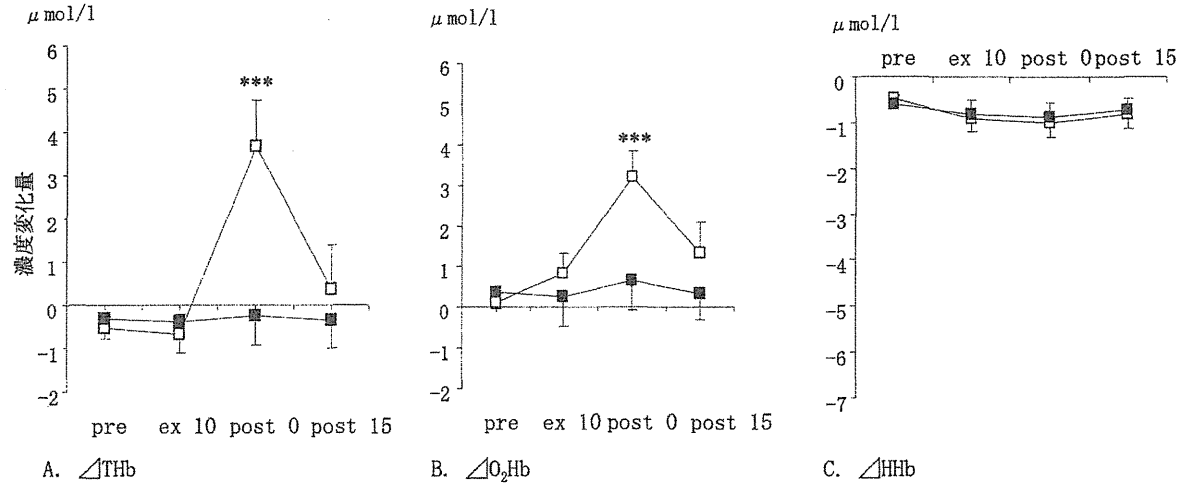

図2 運動または運動イメージによる僧帽筋ヘモグロビン濃度の変化
□：運動群，■：イメージ群，⊿THb：総ヘモグロビン濃度変化量，⊿O_2Hb：酸素化ヘモグロビン濃度変化量
⊿HHb：脱酸素化ヘモグロビン濃度変化量，平均±SE.，*** p<0.001 vs. pre

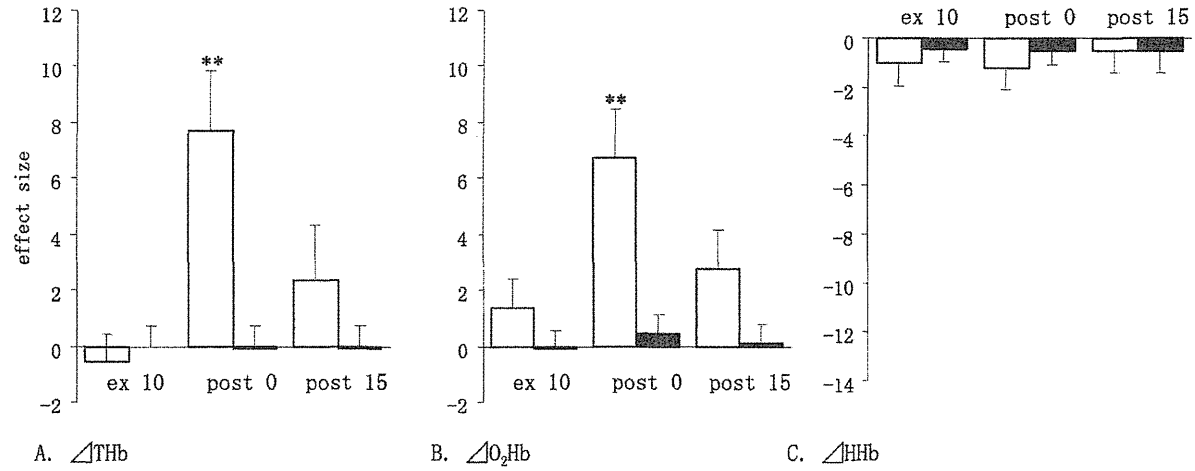

図3 運動または運動イメージによる僧帽筋ヘモグロビン濃度変化量の群間比較
□：運動群，■：イメージ群，⊿THb：総ヘモグロビン濃度変化量，⊿O_2Hb：酸素化ヘモグロビン濃度変化量
⊿HHb：脱酸素化ヘモグロビン濃度変化量，平均±SE.，**p<0.01 vs.イメージ群

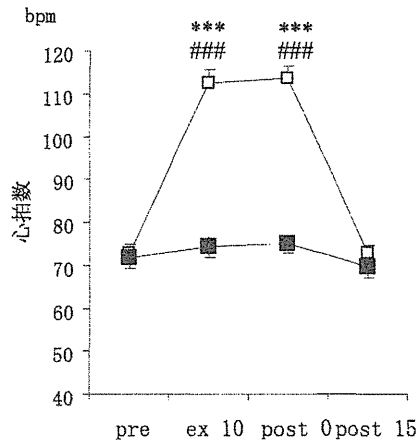

図4 運動または運動イメージによる心拍数の変化
□：運動群，■：イメージ群，平均±SE.，
*** p< 0.001 vs. pre，### p<0.001 vs. イメージ群

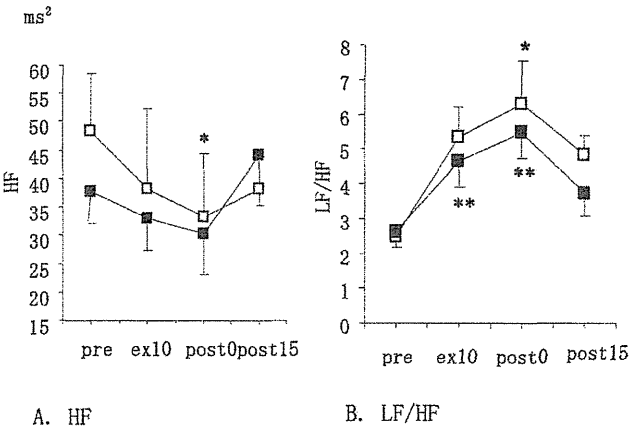

図5 運動または運動イメージによる心拍変動の変化
□：運動群，■：イメージ群，平均±SE.，
*，**p<0.05，0.01 vs. pre

と⊿O_2Hb は post 0 で運動群が有意に高値を示した（図 3A, B)。⊿HHb は両群とも変化しなかった（図 2C, 図 3C)。心拍数は，pre と比べ運動群で ex 10 と post 0 で有意な上昇を示したのに対し，イメージ群は変化せず，また群間比較においても ex 10 と post 0 で運動群が有意に高値を示した(図 4)。HF は，pre と比べ運動群では Post 0 で有意な低下を示したが，イメージ群では変化を示さなかった（図 5A)。LF/HF は，pre と比べ運動群で post 0，イメージ群では ex 10 と post 0 で有意な上昇を示し，群間では差を認めなかった(図 5B)。

考察

実際の自転車駆動運動のみならず，運動イメージを行うことによっても，運動の影響を受けにくい遠隔部の圧痛耐性値が上昇し痛覚感受性の低下を認め，広汎性の疼痛抑制効果が確認された。運動は疼痛のマネジメントとして推奨されており，線維筋痛症や慢性腰痛などの慢性疼痛患者に対する自転車駆動運動は圧痛閾値の上昇や自発痛の減少をもたらすことが報告されている[12,13]。一般に，慢性頚肩痛や腰痛など運動器の疼痛では，筋微小循環障害が原因のひとつと考えられており[14]，20 分間の自転車駆動運動を行うことで主運動部から離れた部位の筋血流を改善し，疼痛を抑制したとの報告もされている[2,15]。しかし，今回の運動イメージでは心拍数の増加を認めていないことから運動は負荷されていないことが確認されている。さらにイメージ群では運動部と離れた僧帽筋において血液循環動態の変化を認めなかったにもかかわらず痛覚感受性が低下したことから，末梢組織の変化が疼痛抑制の要因ではないことが示唆される。

運動による疼痛抑制機序としては，このような末梢組織のコンディショニング効果のみでなく，一次運動野や運動前野，視床の関与が示されている。一次運動野の活動は，GABAergic inhibitory system を活性化することや，視床の活動を抑制することが報告されている[16]。また，経頭蓋磁気刺激などの非侵襲的な脳刺激による運動野の活性化は，視床の過活動と神経の可塑的変化を是正し，これらの効果は視床下部や帯状回，脊髄など他の疼痛関連領域にも伝達されるといわれている[17]。さらに，これらの機序にもとづき，神経因性疼痛や幻肢痛，線維筋痛症のような難治性慢性疼痛患者の運動野を経頭蓋磁気刺激や経頭蓋直流電気刺激によって活性化させることで疼痛が軽減したとの報告も多数されていることから[5,18,19]，運動関連脳領域の活性化が疼痛抑制の重要な因子であると考えられる。

一方，運動イメージは，被験者自身が運動を行っていると感じるような筋感覚的運動イメージである一人称的運動イメージと，他者が運動を行っていることを観察することによる視覚的運動イメージである三人称的運動イメージに分けられる。今回行った運動イメージは，他者の運動を観察しながら自分が運動しているようなイメージを行っていることから一人称的運動イメージと三人称的運動イメージの両要因が含まれていると考えられる。一人称的運動イメージでは，一次運動野，運動前野，前補足運動野，補足運動野，一次体性感覚野など運動実行中とほぼ同じ脳領域が活動することが報告されており[6,7,20]，また三人称的運動イメージによっても一人称的運動イメージと同様に運動前野や補足運動野の活性化を認めるといわれている[21]。これらのことから，運動イメージによっても運動関連脳領域が賦活したことで実運動と同様に痛覚感受性が低下したと考えられる。

また，実際の運動を伴わない運動イメージにおいても実運動と同様に交感神経活動の亢進が認められた。近年 HRV は，認知課題による前頭前野の活動と相関があること[22]，恐怖や不安などの精神的ストレス下において腹内側前頭前野や扁桃体の活動と相関があること，上肢の把握運動中の視床下部，前頭前野，扁桃体，島，中脳水道周囲灰白質の活動と相関があることが示されている[11]。また前帯状回の活動も HRV に反映されることが示されており[23]，HRV は運動関連脳領域の活動のみでなく疼痛関連脳領域の活動とも深い関係性を示すことが示唆される。これらのことから，実際の運動を伴わない運動イメージによる交感神経活動の賦活は，疼痛修飾系の作動トリガーである運動および疼痛関連脳領域の賦活を反映する可能性が示唆される。

このように程度の差はあれども運動イメージは，運動実施時と同様に，広汎な痛覚感受性低下と交感神経活動をもたらしたことから，運動関連脳領域の賦活とともに中枢性疼痛修飾系に影響を及ぼす可能性が示唆された。また，実運動と運動イメージでは筋血液循環動態の変化が異なっていたことから，疼痛抑制機序において筋血液循環動態の変化が特異的な要因であるかは明確でなく，運動や運動イメージによる疼痛抑制には末梢組織のコンディショニングよりも，むしろ中枢性疼痛修飾系が強く関与している可能性が示唆された。

本研究の限界点として，対象が健常者であることから下行性疼痛抑制系に変調をきたしている慢性疼痛有訴者に対する運動や運動イメージの疼痛抑制効果は明らかでない。また，今回の結果では HF が運動群でしか有意な変化を示さなかったことや HRV は注意や集中など心理的ストレスによっても変化する[12]ことより，イメージ群での HRV の変