pain and alexithymia and were therefore assessed and controlled in all analyses. Marital status was classified as never married, divorced, separated, widowed, married, or cohabiting. Educational level was classified as one of three education duration categories: under 9 years, 9–12 years, or over 12 years. Economic status was assessed by a question asking, 'How difficult or easy is your current financial status?' Response options for this question were 'Very hard,' 'Hard,' 'Normal,' 'Easy,' and 'Very easy.' Based on the participant's response, economic status was divided into three classes: low (very hard or hard), average (normal), and high (easy and very easy). Similar one-item questions about economic status have demonstrated validity through their associations with psychological and physical health [25].

3. Statistical analysis

We first computed the means and standard deviations, medians and interquartile ranges (of continuous variables), and rates (of categorical variables) of the study variables for descriptive purposes. To better understand the association between alexithymia and potential confounding factors (i.e., age, sex, marital status, educational level, and economic status), we examined their trend tests using a linear regression analysis, logistic regression analysis, or the Jonckheere-Terpstra test, as appropriate. Logistic regression analysis was used to examine the unadjusted and adjusted odds ratios (ORs) with 95% confidence intervals (CIs) and p for trend of chronic pain according to the TAS-20 score levels taken as categorical variables. In the multivariable-adjusted model, adjustments were made for age, sex, marital status, years of education, and economic status. We estimated the ORs per 1-point increment in the TAS-20 score using the relevant logistic model including the TAS-20 score taken as a continuous variable. The heterogeneity in the association between sexes was tested by adding the interaction term to the relevant logistic model. We also estimated the association (ORs and p for trend) between the quartiles of the TAS-20 subscales and the presence of chronic pain using logistic regression analysis. The trends in the dose-response associations between TAS-20 score levels and the pain intensity, disability, anxiety, depression, and life satisfaction were tested using the Jonckheere-Terpstra trend test for the participants with chronic pain. The SAS software package version 9.2 (SAS Institute, Cary, NC, USA) was used for all analyses. Two-sided values of $p<0.05$ were considered significant in all analyses.

Results

The characteristics of the study sample are summarized in Table 1 as a function of the TAS-20 categories. The prevalence of alexithymic (TAS-20>60) in all participants was 7.8% (n = 72; 35 men, 37 women). There were significant associations between the TAS-20 categories and both education level and economic status, with lower education level and lower economic status associated with higher levels of the TAS-20 categories relative to those with higher education level or economic status. The scores for negative affect, such as depression and anxiety symptoms, were significantly increased with elevating TAS-20 categories. No significant associations were found between the TAS-20 categories and age, sex, or marital status.

Approximately 47% of the participants (n = 439; 152 men, 287 women) were classified as having chronic pain, and 17.9% (n = 166; 41 men, 125 women) were classified as having acute pain. For those with pain, the primary pain sites were the low back (30.1%), shoulders and arms (30.1%), legs (19.6%), head, face, or neck (13.2%), and other sites (7.2%) in the chronic pain group, and shoulders and arms (34.9%), low back (22.9%), legs (16.9%), head, face, or neck (15.0%), back (6.0%), and other sites (4.2%) in the acute pain group. The prevalence of alexithymic turned out to be 4.0% in the painless group, 6.6% in the acute pain group, and 10.9% in the chronic pain group.

The prevalence of pain as a function of the TAS-20 categories is shown in Figure 1. As the scores of the TAS-20 categories increased, the prevalence of chronic pain increased and that of 'no pain' decreased.

Table 2 shows the unadjusted and multivariable-adjusted ORs for the presence of chronic pain according to the TAS-20 categories. Compared with the low-normal alexithymia group, the unadjusted ORs for the presence of chronic pain were significantly higher, around twofold higher, in the high-normal alexithymia and alexithymic groups. After adjusting for age, sex, marital status, years of education, and economic status, this association remained substantially unchanged. Approximately 40% of the participants belonged to these two (high-normal alexithymia and alexithymic) high-risk groups.

As a continuous variable, every 1-point increment in the TAS-20 score was associated with a 1.04-times (95%CI: 1.02–1.06) higher likelihood of the presence of chronic pain after the adjustment for the aforementioned confounding factors. The subgroup analysis stratified by sex showed that the odds ratios in the high-normal alexithymia and alexithymic groups were significant for both sexes, without any evidence of significant heterogeneity in the association between sexes (p for heterogeneity = 0.54).

Because including the participants with acute pain in the group without chronic pain in the present analysis may have underestimated the association, we examined the difference between the chronic pain and no-pain groups only. In these analyses, the odds ratios were even higher in the high-normal alexithymia group (OR: 2.05, 95% CI: 1.40–3.00) and alexithymic group (OR: 3.60, 95% CI: 1.83–7.08). The relationships between TAS-20 categories and chronic pain became nonsignificant after adjusting for depression symptoms (p for trend = 0.57) or for anxiety symptoms (p for trend = 0.57).

Figure 2 presents the odds ratios for chronic pain as a function of quartiles of the TAS-20 subscales score, controlled for demographic factors. There were significant differences between the first quartile and both the third and the fourth quartiles in DIF subscale score. There was also a significant difference between the first quartile and the fourth quartile in DDF subscale score. However, there was no significant association between the EOT subscale score quartiles and the presence of chronic pain. Thus, the TAS-20 DIF subscale demonstrated the strongest association with the presence of chronic pain, although in this sample the TAS-20 DDF subscale may also play a role.

Table 3 shows the association between the TAS-20 categories and pain-related outcomes of the 439 participants with chronic pain. As the level of the TAS-20 categories increased, so did the levels of pain intensity, disability, and depression and anxiety symptoms. The TAS-20 categories were negatively associated with life satisfaction.

Discussion

To our knowledge, this is the first study to examine the association between alexithymia and chronic pain in a sample that is representative of the general population. As hypothesized, we found that alexithymia is significantly associated with a higher prevalence of chronic pain and that this association is mediated by negative affect, such as depression and anxiety symptoms. Also as hypothesized, the TAS-20 subscale assessing difficulty identifying

Table 1. Characteristics of the study population according to the TAS-20 score level.

	Total	TAS-20 score				
		Low-normal	Middle-normal	High-normal	Alexithymic	
		<44	44–50	51–60	>60	p for trend
	n = 927	n = 278	n = 283	n = 294	n = 72	
Sociodemographic characteristics						
Age, year	61±11	60±11	61±11	61±11	63±13	0.10
Women, %	64.8	64.7	66.4	66.7	51.4	0.32
Marital status (married/cohabiting), %	81.8	86.0	78.1	80.6	84.7	0.33
Educational levels (under 9 years), %	17.0	11.2	15.9	21.4	26.4	<0.001
Economic status (low), %	19.6	17.3	16.3	22.8	29.2	0.01
Negative affect						
Depression symptom, score	0.69 (0.46–1.00)	0.54 (0.31–0.77)	0.62 (0.38–0.85)	0.85 (0.62–1.23)	1.31 (0.85–1.77)	<0.001
Anxiety symptom, score	0.40 (0.20–0.70)	0.20 (0.10–0.40)	0.30 (0.20–0.50)	0.60 (0.30–0.80)	1.00 (0.60–1.30)	<0.001

Values are means ± std. dev. or frequencies or median (interquartile range).
The TAS-20: the 20-item Toronto Alexithymia Scale.
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feelings is more closely associated with pain than the other two TAS-20 subscales. We also found that alexithymia was associated with measures of additional pain-related quality of life domains (depression, anxiety, disability, and satisfaction with life) in the subsample of individuals with chronic pain. These findings have important implications for understanding pain and promoting general health.

1. Comparison with previous reports

The prevalence of alexithymic was reported to be approximately 10% in studies based in Finland (age range: 30–97 years) and Germany (age range: 20–69 years) [26,27]. Our prevalence result, 7.8% (age range: 40–91 years), is probably lower because our participants did not include younger people (in their 20 s), who have been reported to have relatively high TAS-20 scores in Japan [18]. Although as far as we know there are no population-based studies on the relationship between alexithymia and chronic pain, there are some hospital-based cross-sectional studies for various patient populations. Most of these studies found a positive association between alexithymia and the presence of chronic pain [15,28–30].

For example, Mehling and Krause reported that scoring in the upper quartile of the alexithymia total score was associated with twofold (adjusted OR = 2.00, 95%CI: 1.31–3.00) higher odds of the 12-month prevalence of low back pain, which was assessed by the medical history taken during the drivers' relicensing exams of 1,180 San Francisco transit operators [8]. These results are consistent with our finding. However, several studies have shown negative [31–33] or mixed correlations [34]. The discrepancy in correlations may be due to differences in health status or study design (e.g., using healthy controls or patient controls).

A population-based prospective longitudinal study [35] was conducted with the same population as that in the aforementioned cross-sectional study by Mehling and Krause [8]. The longitudinal

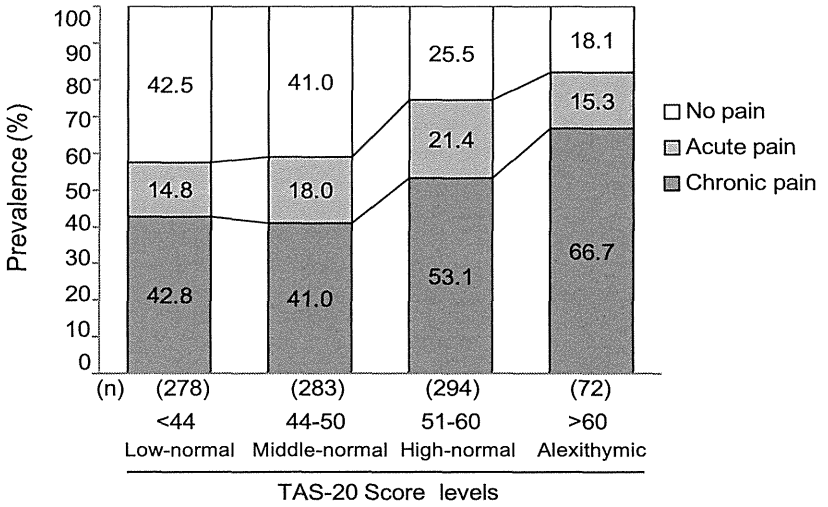

Figure 1. Self-reported pain prevalence according to the TAS-20 score levels in a general population from the Hisayama Study health survey. Acute pain: <6 months of pain. Chronic pain: pain that had been experienced for 6 months or longer.
doi:10.1371/journal.pone.0090984.g001

Table 2. Odds ratios for chronic pain according to the TAS-20 category score.

	TAS-20 score	Number of participants	Number with Chronic pain	Unadjusted			Multivariable-adjusted		
Alexithymia level				**OR (95%CI)**	**p value**	**p for trend**	**OR (95%CI)**	**p value**	**p for trend**
Total									
Low-normal	<44	278	119	1.00 (reference)			1.00 (reference)		
Middle-normal	44–50	283	116	0.93 (0.66–1.30)	0.66	<0.001	0.91 (0.65–1.28)	0.6	<0.001
High-normal	51–60	294	156	1.51 (1.09–2.10)	0.01		1.49 (1.07–2.09)	0.02	
Alexithymic	>60	72	48	2.67 (1.55–4.61)	<0.001		2.56 (1.47–4.45)	0.001	
Men									
Low-normal	<44	98	40	1.00 (reference)			1.00 (reference)		
Middle-normal	44–50	95	38	0.97 (0.54–1.72)	0.91	0.007	0.96 (0.54–1.72)	0.9	0.01
High-normal	51–60	98	51	1.57 (0.89–2.77)	0.12		1.56 (0.88–2.77)	0.13	
Alexithymic	>60	35	23	2.78 (1.24–6.22)	0.01		2.55 (1.12–5.82)	0.03	
Women									
Low-normal	<44	180	79	1.00 (reference)			1.00 (reference)		
Middle-normal	44–50	188	78	0.91 (0.60–1.37)	0.64	0.004	0.89 (0.58–1.35)	0.58	0.005
High-normal	51–60	196	105	1.48 (0.97–2.22)	0.06		1.48 (0.98–2.25)	0.06	
Alexithymic	>60	37	25	2.66 (1.26–5.63)	0.01		2.59 (1.21–5.53)	0.01	

OR: odds ratio; CI: confidence interval.
Multivariable adjustment was made for age, gender, marital status, years of education and economic status. In the stratified analyses of gender, ORs were not adjusted for gender.
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study revealed a negative association between alexithymia and the 7.5-year incidence of compensated claims for low back pain, which was assessed by physician-confirmed diagnoses from administrative workers' compensation data. As the authors mentioned, a possible interpretation of their results is that alexithymic patients with chronic pain were unlikely to complain by filing a workers' compensated claim for low back pain injury because of their fear of being shamed and self-devaluated and/or their shyness and anxiety concerning the verbal expression of their emotions. Further prospective longitudinal studies with an appropriate method for estimating chronic pain are warranted.

2. Alexithymia, negative affect, and pain

Alexithymia is a personality trait associated with poor emotional awareness and affect regulation [9]. Our present findings confirm that this trait — in particular the aspect of alexithymia that involves having difficulty identifying one's feelings — is associated with the presence of chronic pain in the general population. This association also becomes nonsignificant when negative affect is controlled, suggesting that negative feelings such as depression and anxiety may mediate the association between alexithymia and chronic pain. This pattern of findings is consistent with previous

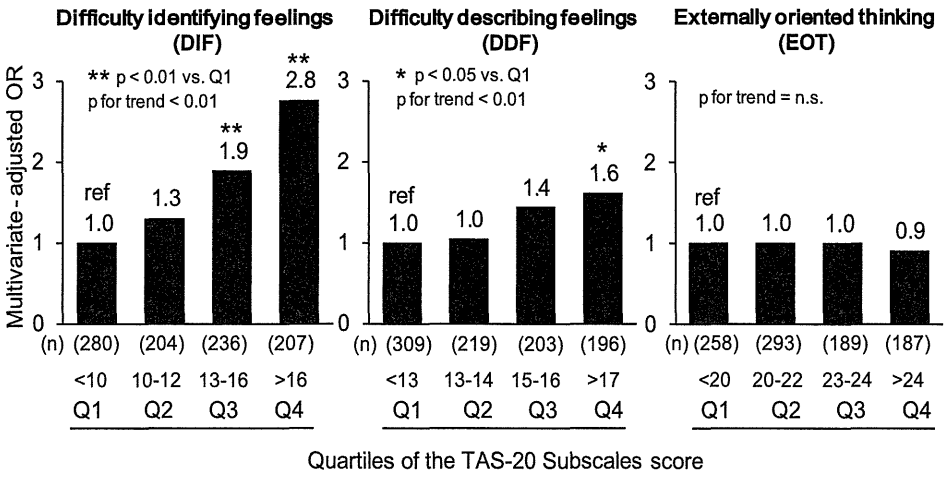

Figure 2. Odds ratios for chronic pain according to the TAS-20 subscales, adjusted for demographic factors in the general population.
doi:10.1371/journal.pone.0090984.g002

Table 3. The relationship between the TAS-20 score levels and the pain-related outcomes of the 439 participants with chronic pain.

	TAS-20 score				
	Low-normal	Middle-normal	High-normal	Alexithymic	
	<44	44–50	51–60	>60	p for trend
	n = 119	n = 116	n = 156	n = 48	
Pain intensity, mm	30 (15–50)	44 (20–54)	47 (24–65)	58 (36–80)	<0.001
Disability, mm	5 (0–15)	15 (0–31)	10 (0–38)	29 (3–61)	<0.001
Depression, score	0.7 (0.4–0.8)	0.7 (0.5–1.0)	0.9 (0.6–1.3)	1.4 (1.2–1.9)	<0.001
Anxiety, score	0.3 (0.2–0.6)	0.4 (0.2–0.6)	0.6 (0.4–0.8)	1.1 (0.8–1.6)	<0.001
Life satisfaction, mm	75 (50–89)	65 (47–81)	51 (40–71)	50 (38–61)	<0.001

Values are medians (interquartile range).
Pain intensity, disability and life satisfaction were evaluated by Visual Analogue Scale.
Depression and anxiety scores were evaluated by Symptom Check List-90-R.
doi:10.1371/journal.pone.0090984.t003

research involving samples of individuals with chronic pain [13,36].

In addition, our finding that the DIF and DDF domains of the TAS-20 were associated with the likelihood of chronic pain, while the EOT domain was not, is consistent with the findings of previous studies examining alexithymia and pain [7,8,11,14]. The finding may be due to poor reliability of the EOT subscale [37]. Given the cross-cultural consistency of the finding, however, it does not appear to be due to language issues or cultural differences.

3. Possible mechanism underlying the association between alexithymia and chronic pain

Various theories linking alexithymia and physical illness have been conceptualized at the physiological level (e.g., the hypothalamic-pituitary-adrenal axis, chronic sympathetic hyperarousal, inflammation, and impaired immune status), the behavioral level, and the cognitive level (e.g., illness behavior, somatic amplification) [38,39]. Some neuroimaging studies of alexithymia and chronic pain have been conducted recently, and their findings may contribute to our understanding of the mechanism of the relationship. First, neuroimaging data indicate not only hyperactivity in pain perception areas such as the insular cortex, but also hypoactivity in pain-processing regulatory areas such as the prefrontal cortex. Lack of an emotional regulation system might cause hypersensitivity to aversive bodily sensations and prolonged, pain-related affective reactions such as distress [40,41]. Second, a possibility is related to the known negative effect of depression on the descending inhibitory system [42]. That is, alexithymia may lead to increased risk of depression, which may then interfere with an individual's ability to reduce or inhibit pain.

4. Clinical implications

Our analyses of the subgroup of participants with chronic pain supported a link between alexithymia and a number of measures of the key functioning domains in these individuals, including pain intensity, disability, depression and anxiety (positive associations), and life satisfaction (negative association). To the extent that these associations are causal — a conclusion that cannot yet be drawn due to the correlational nature of the current and previous findings — then treatments that decrease alexithymia could potentially have significant benefits across multiple quality of life domains for individuals with chronic pain. Thus, our findings support the need for research to develop and test interventions [43,44] that could help individuals identify and describe their feelings, and to determine whether these interventions promote health-related quality of life and reduce the risk for chronic pain as a general health policy.

5. Study strengths and limitations

The study has a number of important strengths, including its large sample size and a population-based study design. Some limitations should be noted, however.

One primary limitation is that the data are cross-sectional. We thus cannot conclusively determine if alexithymia influences the presence and severity of negative affect and pain, if negative affect and pain influence alexithymia, or if there is an unidentified third variable that influences all three. However, experts generally agree that alexithymia is a trait that develops early in life and that it rarely changes without active intervention [45]. Thus, the possibility that alexithymia has a greater impact on pain and depression than these variables have on alexithymia remains viable. Prospective longitudinal studies are needed to clarify the contribution of alexithymia to the development of chronic pain and other negative outcomes. A second limitation is related to the possibility of selection bias, because approximately one-half of the individuals who participated in the regular Hisayama Study survey did not participate in our research. Certainly, we cannot deny the possibility that people with physical or mental complaints were more willing to participate in the study than were people without. In contrast, health-conscious people might have been more likely to participate in the study than non-health-conscious people. The fact that the present study population had many more females than males (601 women, 326 men) may support these possibilities [46]. Therefore, the generalizability of our findings to all individuals in the community may be limited. Nevertheless, we believe that our findings provide important information to consider alexithymia as a cognitive factor that may exacerbate physical symptoms such as chronic pain. Third, our questions about the presence of chronic pain have not clearly determined temporal patterns of chronic pain (e.g., it is unclear how a patient with recurrent pain would respond to the questions). A fourth limitation is that the causes of pain were not assessed in this study. It will be informative to explore whether or not the magnitude of the associations between alexithymia and chronic pain is different between participants with pain disorders that have or do not have

one or more established biological causes. However, this limitation is unlikely to alter our conclusion, because previous studies have shown a positive correlation between alexithymia and pain-related outcomes regardless of the presence or absence of biological cause [12,26,27,44,47]. Lastly, pain intensity, disability, and life satisfaction were each assessed with a single-item measure using a VAS, which may have limited reliability of a part of the results compared to assessment that uses multiple-item questionnaires.

Conclusions

The results of the present study indicate that alexithymia is significantly associated with a greater prevalence of chronic pain in the general population and that individuals with alexithymia have more pain intensity, disability, and depression and anxiety symptoms, and less life satisfaction than those without alexithymia. Our findings highlight certain clinically important concepts; i.e., that adverse psychological factors and personality traits play a significant role in the etiology of chronic pain. The early identification of alexithymia and negative affect may be beneficial in preventing chronic pain and reducing the clinical and economic burdens of chronic pain. Further prospective studies and interventional studies are needed to confirm this hypothesis.

Supporting Information

Figure S1 Flow chart of the participant recruitment. (EPS)

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Author Contributions

Conceived and designed the experiments: MS MH. Performed the experiments: MS MH KA SM RI K. Yamashiro TY YI. Analyzed the data: MS TN K. Yonemoto YK. Contributed reagents/materials/analysis tools: MS MH. Wrote the paper: MS TN MPJ KA CK NS YK MH.

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ORIGINAL ARTICLE

Prevalence of neuropathic pain in cases with chronic pain related to spinal disorders

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Abstract
Background The incidence and characteristics of neuropathic pain associated with spinal disorders have not yet been fully clarified. The purpose of this study was to investigate the prevalence of neuropathic pain and the degree of deterioration of quality of life (QOL) in patients with chronic pain associated with spinal disorders who visited orthopedic outpatient clinics.
Methods This cross-sectional study was conducted in 1,857 patients recruited from 137 medical institutions nationwide. Participants were men and women aged 20–79 years with a history of spine-related pain for at least 3 months and a visual analog scale (VAS) score of at least 30 in the previous week. Patients were screened using a neuropathic pain screening questionnaire. The degree of QOL deterioration and its correlation with the presence of neuropathic pain were assessed using the Short Form Health Survey with 36 questions (SF-36).
Results Overall prevalence of neuropathic pain was 53.3 %. It was relatively high in patients with cervical spondylotic myelopathy (77.3 %) and ligament ossification (75.7 %) and relatively low in those with low back pain (29.4 %) and spondylolysis (40.4 %). Only 56.9 % of patients with radiculopathy were diagnosed with neuropathic pain. Logistic regression analysis identified several risk factors, including advanced age, severe pain, disease duration of at least 6 months, and cervical lesions. In QOL assessment, physical functioning, role-physical, role-emotional, and social functioning were severely affected, and this trend was more pronounced in patients who were more likely to have neuropathic pain.
Conclusions The frequency of neuropathic pain tended to be higher in patients with diseases associated with spinal cord damage and lower in patients with diseases that primarily manifested as somatic pain. A bias toward allodynia symptoms in the screening questionnaire may have resulted in the failure to diagnose neuropathic pain in some patients with radiculopathy. Poor QOL, primarily from the aspect of physical functioning, was demonstrated in patients with neuropathic pain associated with spinal disorders.

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Introduction

A significant number of people in the general population appear to suffer from chronic pain arising from the musculoskeletal system. According to a survey conducted by Nakamura et al. [1], 15.4 % of Japanese adults have chronic pain arising from the musculoskeletal system. The most commonly affected site (65 %) is the lumbar region, followed by neck and shoulder regions (55 % each), indicating a high incidence of chronic pain related to disorders of the spine.

Based on the mechanism of pain onset, chronic musculoskeletal pain has been classified into two types:

(1) chronic nociceptive pain arising from deformation and inflammation of the bone(s), joint(s) and/or other spinal tissues; and (2) neuropathic pain caused by damage to nerve tissues per se. Spinal disorders often involve damage to nerve tissues, such as the spinal cord, nerve roots, and cauda equina, which gives rise to neuropathic pain. Neuropathic pain may also occur concurrently with nociceptive pain arising from involvement of intervertebral discs and paraspinal muscles. However, incidence and clinical features of neuropathic pain associated with spinal disorders have not yet been clearly elucidated.

Under the initiative of the Japanese Society for Spine Surgery and Related Research (JSSR), a study was conducted to determine the prevalence of neuropathic pain and the degree of quality of life (QOL) deterioration in patients with chronic pain associated with spinal disorders who visited orthopedic outpatient clinics in Japan. Results are reported herein.

Patients and methods

This was a cross-sectional study conducted on outpatients recruited from 137 Japanese medical institutions. Participant institutions were required to employ at least one board-certified spine surgeon approved by JSSR and to be an orthopedic hospital with at least 20 beds, a general hospital, or a university hospital. Participating institutions were selected from regions throughout the country: ten from Hokkaido, nine from Tohoku, ten from North Kanto, 35 from South Kanto, 11 from Tokai, seven from Hokuriku, 24 from Kansai, 13 from Chugoku-Shikoku, and 18 from Kyushu. The number of institutions was allocated according to the number of approved surgeons in each geographical area, with 10–20 patients recruited from each institution. The study was initiated in March 2010 and completed in November of the same year. The study protocol was approved by the institutional ethics committee of each participating institution.

Participants

The study participants were patients judged by spine surgeons to meet all of the following criteria:

1. Chronic pain persisting for at least 3 months
2. Spine-related pain (including in those who have undergone surgery)
3. Visual analogue scale (VAS) score of at least 30 during the previous 1 week
4. Age 20–79 years
5. Capable of filling out the questionnaire in Japanese without assistance

Table 1 Patient background characteristics

Patient variables	Corresponding statistics
Male gender (%)	50.4
Age (years)	63.4 ± 12.6
Body weight (kg)	60.4 ± 11.8
Height (cm)	159.7 ± 9.1
Body mass index (kg/m^2)	23.6 ± 3.6
Current pain (VAS; mm)	54.0 ± 25.0
Duration of pain (months)	47.4 ± 62.1
Median (min–max)	26 (3–600)
Level of the spinal disorder	
Cervical	324 (17.4 %)
Thoracic	108 (5.8 %)
Lumbar	1,537 (82.8 %)
Sacral	7 (0.4 %)
Medical therapy	
Medication	
NSAIDs	1,442 (77.7 %)
Opioids	70 (3.8 %)
Anticonvulsants	174 (9.4 %)
Antidepressants	167 (9.0 %)
Steroids	42 (2.3 %)
Prostaglandins	148 (8.0 %)
Others	200 (10.8 %)
Nerve block	553 (29.8 %)
Physical therapy	325 (17.5 %)
Psychological therapy	14 (0.8 %)

VAS visual analog scale, *min* minimum, *max* maximum, *NSAIDs* nonsteroidal anti-inflammatory drugs

Patients meeting any of the following criteria were excluded from the study:

1. History of receiving nerve-block therapy in the previous 6 months
2. Pain arising from the spine, as well as from other tissues/organs
3. Being an inpatient
4. Severe paralysis
5. Incapable of giving consent due to the presence of complications

A total of 2,025 patients were recruited from 137 institutions. Of these, 168 were excluded from the study for the following reasons: not willing to provide informed consent for participation (13); history of pain for ≤3 months (36); ≥80 years (68); VAS data not available or scores ≤30 (29); data from the neuropathic pain screening questionnaire not available (22). The remaining 1,857 patients were entered into the study. Table 1 summarizes the characteristics of study participants. The patient population consisted of an almost equal number of men and women. Elderly patients predominated,

Table 2 Spinal disorders

	Number (%)
Degenerative disorders	1,586
Lumbar spinal stenosis	742 (40.0)
Intervertebral disc disorders	358 (19.0)
Degenerative spondylolysis	197 (10.6)
Spondylosis	170 (9.2)
Cervical spondylotic myelopathy	110 (5.9)
Nerve root damage	65 (3.5)
Spondylolysis	50 (2.7)
Low back pain	17 (0.9)
Ligament ossification	91 (4.9)
Spine/spinal cord injury	77 (4.1)
Iatrogenic spinal disorder	75 (4.0)
Spine/spinal cord tumor	38 (2.0)
Osteoporosis	15 (0.8)
Infectious spondylitis/intervertebral discitis	9 (0.5)
Other types of spondylitis	15 (0.8)
Other types of neurological disorders	11 (0.6)
Unknown	13 (0.7)
Total	1,857

Some patients were diagnosed as having more than one of these conditions; therefore, the sum of the number of patients with each diagnosis is larger than the study population

particularly patients in their 70s; mean age was 63.4 years. Mean duration of illness was 47.4 months, with 203 patients having chronic pain for at least 120 months. Mean VAS pain score was 54 mm. The most commonly affected region was lumbar (1,537 cases), followed by cervical (324 cases), thoracic (108 cases), and sacral (7 cases) regions.

Spinal disorder details are shown in Table 2. Degenerative disorders accounted for the majority (1,586) of cases, and the most common diagnosis was lumbar spinal stenosis (742 cases). Iatrogenic spinal disorder refers to residual pain present after spine surgery, such as in cases of multiple operated back and failed back surgery syndrome.

Method

Each patient signed an informed consent form, then filled out the questionnaires regarding pain and health status. The neuropathic pain screening questionnaire, developed by Ogawa et al. [2], was used for the pain survey. When the study began, this questionnaire was the only screening tool for neuropathic pain available in Japanese. Patients' answers to the seven-question domains were weighted and scored (Table 3). The likelihood of neuropathic pain was determined based on total score, as follows: ≥ 5 = highly likely to have neuropathic pain (++); 4 = likely to have neuropathic pain (+); 3 = possibility of neuropathic pain (±); ≤ 2 or lower = unlikely to have neuropathic pain (−). A total score ≥ 4 (+ and ++) was judged as representing neuropathic pain. According to an analysis conducted by Ogawa et al. [2], ratings of + and ++ have an 87.7 % sensitivity and 71.7 % specificity for the presence of neuropathic pain.

Table 3 Questions on the nature of pain

Question		Number	Slight	Moderate	Sever	Very severe
Q1	There is a pinprick-like pain	1	1	1	1	0
Q2	There is an electric shock-like pain	0	0	0	0	1
Q3	There is a tingling burning pain	0	1	1	1	1
Q4	There is a pain with strong numbness	0	1	1	1	1
Q5	Only a light touch with clothing or cold wind causes a pain	0	1	3	3	3
Q6	Site of pain has decreased or increased sensation	0	1	1	1	1
Q7	Site of pain shows skin swelling and/or discoloration to red or purple	0	0	0	1	1

Logistic regression analysis was performed using factors with the potential to affect the result of judgment on the presence/absence of neuropathic pain in order to identify the risk factors for a ++ result. Variables were gender, age, severity of the current pain (VAS), duration of pain, and level of the spinal disorder.

The Short Form Health Survey with 36 items (SF-36) was used for health status. For each SF-36 subscale—physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, mental health—raw scores were calculated and converted to the 0–100 scoring system and then to the norm-based scoring [mean of the Japanese national standard is 50, with a standard deviation (SD) of 10] [3–5]. Possible correlations between assessment results for neuropathic pain and scores for individual subscales of tge SF-36 were assessed. Statistical analysis was performed using the software R 2.13.0

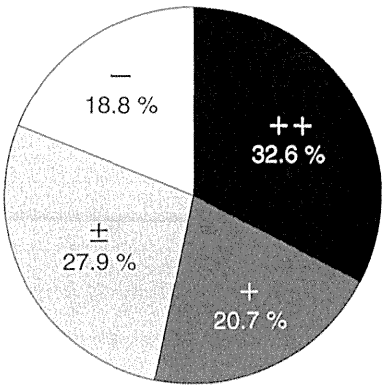

Fig. 1 Prevalence of neuropathic pain: ++ highly likely; + likely; ± possibility; − unlikely

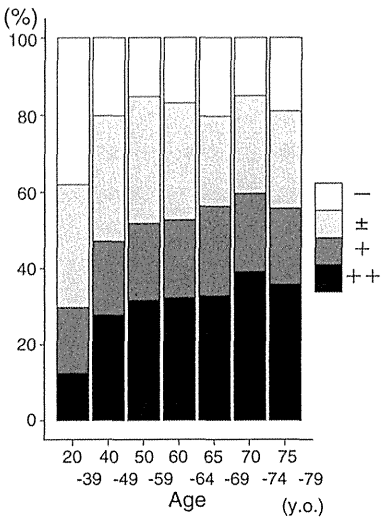

Fig. 2 Correlation between neuropathic pain and age

(R Foundation for Statistical Computing, Department of Statistics and Mathematics Wirtschafts Universitat, Wien, Austria).

Results

Prevalence of neuropathic pain

Results of neuropathic pain assessment was + in 20.7 %, and ++ in 32.6 % of the 1,857 participants. Overall, the prevalence of neuropathic pain was 53.3 % (Fig. 1).

Correlation between assessment of neuropathic pain and patient background factors

The incidence of neuropathic pain tended to increase with advancing age in both men and women. In particular, the incidence was lower in patients in their 20s and 30s and higher in those aged 70–74 years (Fig. 2).

The incidence of neuropathic pain also increased with increasing severity of ongoing pain and duration of illness. Neuropathic pain was most frequently associated with cervical spinal disorder, followed by disorders of the thoracic, lumbar, and sacral regions (Fig. 3). We found no clear correlation between assessment results and body weight or body mass index (BMI).

When we examined the correlation between diagnosis (type of spinal disease) and assessment results, the incidence of neuropathic pain was the highest in patients diagnosed as having cervical spondylotic myelopathy (77.3 %), followed by patients with ligament ossification (75.7 %), iatrogenic spinal disorder (68.0 %), and spine/spinal cord injury (65.0 %). On the other hand, the incidence was low in patients with low back pain (29.4 %) and spondylolysis/spondylolisthesis (40.4 %) (Fig. 4).

Correlation between assessment of neuropathic pain and type of medical treatment received

Nonsteroidal anti-inflammatory drugs (NSAIDs) were the most commonly used pain medications in all patients with chronic pain. Anticonvulsants and antidepressants were used at a higher frequency in the ++ group (Fig. 5). The frequency of nerve-block or physical therapy was not correlated with results of assessment of neuropathic pain.

Factors affecting the of judgment on presence/absence of neuropathic pain

Table 4 presents the odds ratios (OR) calculated by logistic regression analysis of factors for the presence of neuropathic pain rated as ++. As no marked differences were observed between ORs based on the simple correlation (Not adjusted, in Table 4) and those based on multiple regression analysis (Adjusted, in Table 4), these factors were considered to be independent.

Gender had no effect on assessment results of neuropathic pain. Multiple regression analysis by age showed that the OR was 2.72 for the age group 41–69 years and 3.75 for those aged ≥70 years vs the age group ≤40 years; thus, the ratio increased with age. As for pain severity, OR for VAS scores 10 to <50 vs <10 was 2.33; furthermore, OR doubled for VAS scores 50 to <80 and doubled again for VAS scores ≥80. OR was 1.73 for pain duration ≥6 months vs <6 months. OR for cervical-level involvement vs lumbar/sacral-level involvement was 3.20.

Correlation between degree of QOL deterioration and neuropathic pain severity

All participants in had scores below the Japanese standard value of 50 on all SF-36 subscales. By subscale, physical

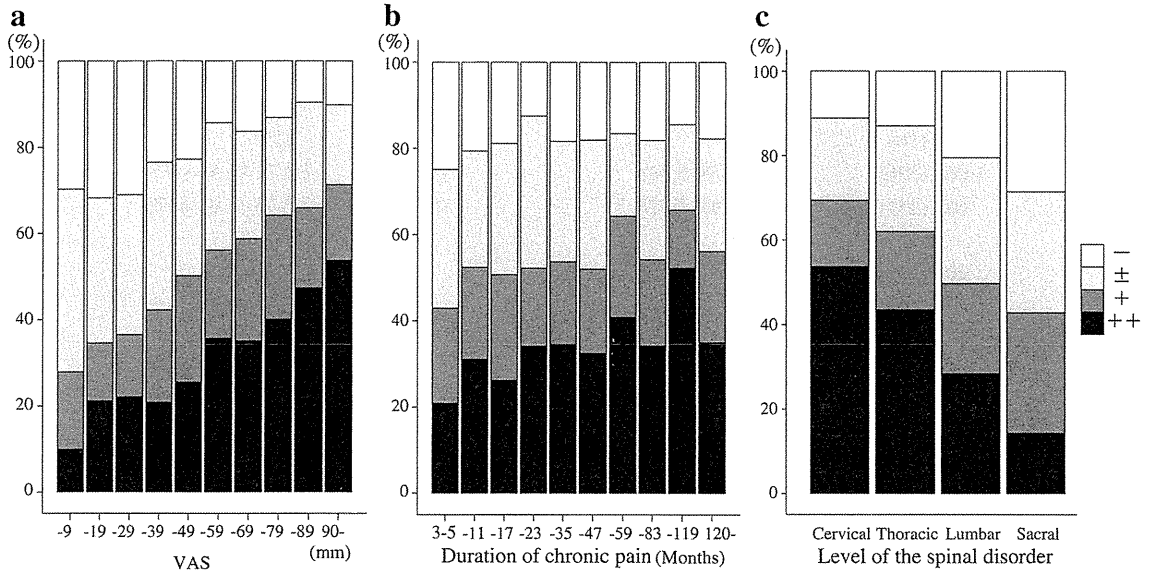

Fig. 3 Correlations between neuropathic pain and pain severity (**a**), duration (**b**), and level of the spinal disorder (**c**)

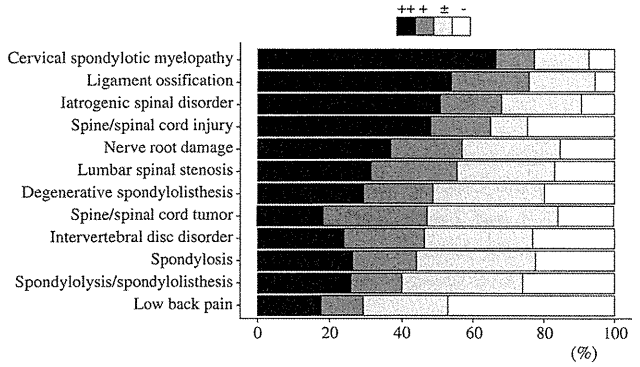

Fig. 4 Correlation between neuropathic pain and diagnosis

functioning, role-physical and role-emotional), and social functioning were more severely affected, a trend that was more pronounced in patients who were more likely to have neuropathic pain (Fig. 6).

Discussion

According to the International Association for the Study of Pain, neuropathic pain is defined as pain caused by a lesion or disease of the somatosensory nervous system. A representative example of neuropathic pain associated with

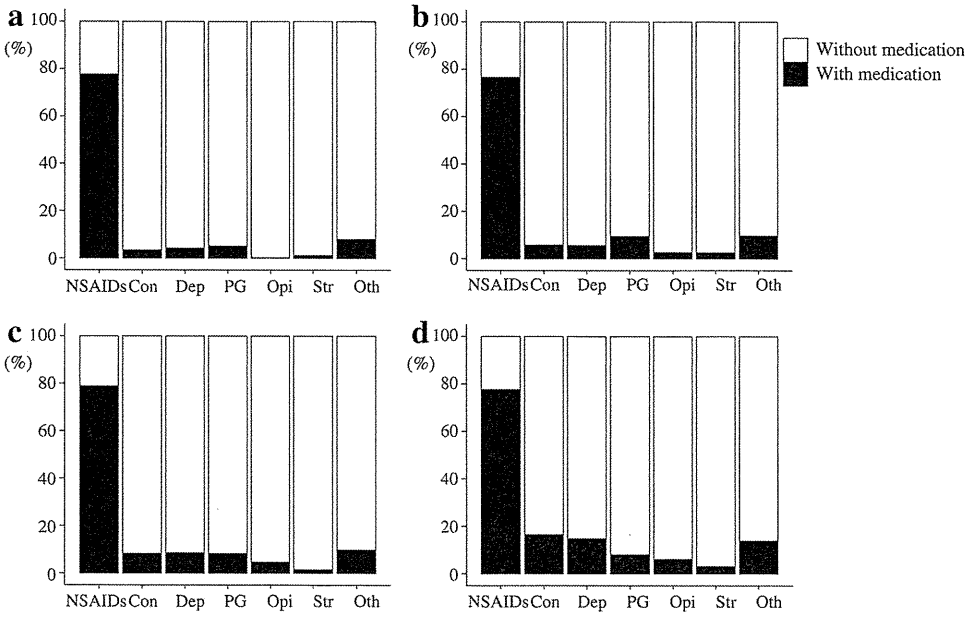

Fig. 5 Correlation between neuropathic pain and pain relief medication used: judgment − (**a**), judgment ± (**b**), judgment + (**c**), judgment ++ (**d**). *NSAIDs* nonsteroidal anti-inflammatory drugs, *Con* anticonvulsants, *Dep* antidepressants, *PG* prostaglandins, *Opi* opioids, *Str* steroids, *Oth* others

Table 4 Risk factors for the presence of neuropathic pain identified by logistic regression

	No. (++)	Not adjusted OR (95 % CI)	*P* value	Adjusted OR (95 % CI)	*P* value
Age					
≤40 years	128 (16)	1.00		1.00	
41–69 years	1,060 (338)	3.23 (1.88–5.54)	<0.001	2.72 (1.56–4.75)	<0.001
70–79 years	669 (251)	4.19 (2.43–7.22)	<0.001	3.75 (2.14–6.58)	<0.001
Gender[a]					
Female	920 (305)	1.00		1.00	
Male	934 (299)	0.95 (0.78–1.15)	0.600	0.90 (0.73–1.11)	0.319
Current pain score (VAS)[a]					
<10 mm	111 (11)	1.00		1.00	
10 to <50 mm	657 (151)	2.71 (1.42–5.19)	0.003	2.33 (1.21–4.51)	0.012
50 to <80 mm	783 (290)	5.35 (2.82–10.13)	<0.001	4.62 (2.41–8.84)	<0.001
80 to <100 mm	303 (152)	9.15 (4.72–17.74)	<0.001	8.35 (4.26–16.36)	<0.001
Pain duration					
<6 months	249 (52)	1.00		1.00	
≥6 months	1,608 (553)	1.99 (1.44–2.74)	<0.001	1.73 (1.23–2.43)	0.002
Level of spinal disorder[a,b]					
Cervical	324 (174)	3.03 (2.37–3.88)	<0.001	3.20 (2.45–4.16)	<0.001
Thoracic	87 (35)	1.52 (0.84–2.74)	0.168	1.65 (0.89–3.05)	0.112
Lumbar/sacral	1,439 (392)	1.00		1.00	
P value					<0.001
Pseudo R^2					0.162

OR odds ratio, *CI* confidence interval, *VAS* visual alanog scale, ++; highly likely to have neuropathic pain, *Not adjusted* OR calculated by each category, *Adjusted* OR calculated using all the listed all covariates, *pseudo-R^2* Cragg and Uhler's pseudo-R^2

[a] Data on gender, current pain score, and level of spinal disorder were lacking in 3, 3, and 7 patients, respectively

[b] Cervical level, patients with cervical-level disorder with/without disorder at other levels; thoracic level, patients with thoracic-level disorder with/without lumbar/sacral level disorder but no cervical-level disorder; lumbar/sacral level, patients with only lumbar/sacral-level disorder

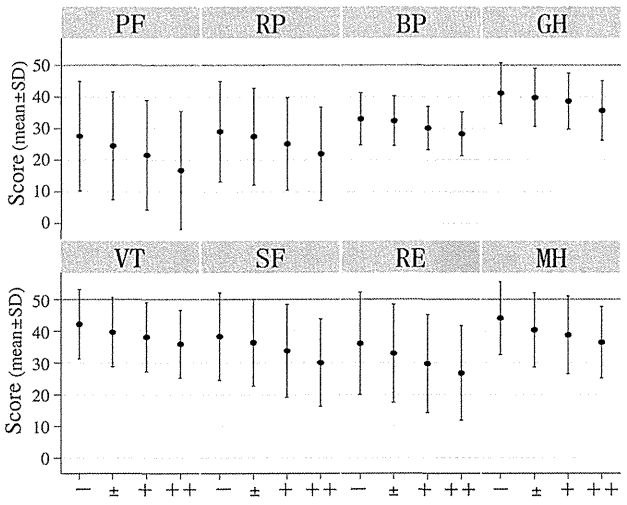

Fig. 6 Correlation between neuropathic pain and degree of quality of life (QOL) deterioration. *PF* physical functioning, *RP* role-physical, *BP* bodily pain, *GH* general health, *VT* vitality, *SF* social functioning, *RE* role-emotional, *MH* mental health

spinal disorders includes pain caused by compression or damage to the spinal cord or the nerve roots.

In their review, Sadosky et al. [6] reported the incidences of neuropathic pain in various diseases as follows: herpes zoster (postherpetic neuralgia) 7–27 %; diabetes (diabetic neuropathy) 9–22 %; cerebral stroke (poststroke pain); 8–11 %; spinal cord injury (postspinal cord injury pain) 10–80 %. Compared with their data, the incidence of neuropathic pain of 53.3 % in our survey of patients with spinal disorders is relatively high. However, our participants were limited to those who had chronic pain for at least 3 months, and the incidence may have been lower if we had also included spinal disorder patients who did not have a history of pain for such a long period of time.

Logistic regression analysis was carried out in this study to identify risk factors for the presence of neuropathic pain rated as ++. Specificity is important for a logistic analysis in order to identify factors predictive of neuropathic pain. Ogawa et al. [2] reported that when the screening score was

≥4 (i.e., corresponding to ratings of + or ++), specificity and sensitivity were 71.7 % and 87.7 %, respectively, which is appropriate for screening but insufficient for a logistic regression analysis. In contrast, the specificity of 89.1 % for a score ≥5 (i.e., corresponding to a rating of ++) is appropriate to conduct a logistic regression analysis. In our study, variables used in the logistic regression analysis were gender, age, severity of current pain (VAS), duration of pain, and level of the spinal disorder. The basic analysis showed no strong correlations among these variables. Logistic regression analysis identified the following risk factors for the presence of neuropathic pain: advanced age, severe pain, disease duration of at least 6 months, and a cervical-level lesion. These results indicate that the more severe the damage to the nerve tissue, the higher the incidence of neuropathic pain.

In the survey of medical treatments, NSAIDs were by far the most frequently used medications overall (~77 %). NSAIDs are effective for relieving nociceptive pain but are considered to be ineffective, in principle, for treating neuropathic pain. Anticonvulsants, which are effective in treating neuropathic pain, were used slightly more often in the ++ group than in the other groups, but the proportion was still only about 16 %. In October 2010, when our study was about to be completed, the anticonvulsant drug pregabalin was approved in Japan for insurance-covered treatment of peripheral neuropathic pain. Therefore, its may have increased after this study in the patients who were evaluated as having neuropathic pain.

When data were summarized by disease, the incidence of neuropathic pain was low in conditions such as low back pain and spondylolysis, which, as the names themselves indicate, represent spinal-tissue-related pain, i.e., somatic pain. The incidence was high in diseases such as cervical spondylotic myelopathy and spine/spinal cord injury, the names of which suggest neuropathic conditions. However, only 57 % of patients with nerve root damage were diagnosed as having neuropathic pain. According to the above-mentioned definition by the International Association for the Study of Pain, patients with nerve root damage (radiculopathy) should always be diagnosed as having neuropathic pain, because the name of the disease itself suggests it. This discrepancy between disease name and diagnosis results can be attributed to the characteristics of the neuropathic pain screening questionnaire we used in the survey. The questionnaire comprised seven components that were biased toward allodynia symptoms, such as "Only a light touch with clothing or cold wind causes a pain," and "There is a tingling, burning pain." However, in actual clinical situations, allodynia symptoms are less frequently seen in cases of nerve root damage associated with intervertebral disc herniation, etc. In the future, we anticipate the development of a diagnostic tool that can be applied for neuropathic pain both with and without allodynia.

On the other hand, approximately 30 % of patients with low back pain were diagnosed as having neuropathic pain, although low back pain manifests primarily as somatic pain via nociceptive mechanisms. Therefore, this result also indicates a limitation of this screening tool in that patients with nociceptive pain may receive a diagnosis of neuropathic pain if allodynia-like symptoms are present. However, low back pain may be associated with neuropathic pain in some cases when some kind of damage to the peripheral nervous tissues in the lumbar spine and surrounding areas is present or neuroplastic changes have developed in the synapses of the dorsal horn of the spinal cord as a result of prolonged afferent nociceptive signals (central sensitization). Freynhagen et al. [7] reported that 37 % of patients with chronic low back pain had some factor suggestive of neuropathic pain. Because our study assessed only 17 patients with low back pain, additional studies with a larger sample size of participants with low back pain are warranted.

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痛みの疫学

慢性疼痛の疫学

The epidemiology of chronic pain

山下敏彦
Toshihiko Yamashita

世界的に高い慢性疼痛有病率

2008～2009年の米国におけるインターネットを用いた大規模調査では，18歳以上の国民の慢性疼痛有病率は30.7%に上っている[1]．ヨーロッパ諸国における調査でも，2004年のフランスでの調査では31.7%[2]，2006～2008年のノルウェーでの調査では31%[3]，2007～2008年のポルトガルでの調査では36.7%[4]，といずれも高い有病率が示されている．このほか，2009～2010年のブラジルでの調査でも有病率は42%と高くなっている[5]．

わが国においても，20歳以上の国民における慢性疼痛有病率は，2009年の松平ら[6]の調査では22.9%，2010年の矢吹ら[7]の調査では22.5%（推定患者数2,315万人）と高い数値が示されている．

このように，とくに最近の疫学調査において，地域を問わず世界的に慢性疼痛の有病率が高いことが明らかになっている．

慢性疼痛の特徴

国内外のいずれの調査においても，慢性疼痛の有病率は，性別では女性で高く，年齢では若年層よりも中高年層で高くなることが示されている．松平ら[6]の調査では，40歳代の女性で最も有病率が高かったとしている．

慢性疼痛の部位としては，すべての報告に共通して，腰が圧倒的に多く（26～64%），すなわち慢性腰痛がきわめて多いことを表している．腰に次いで，膝，肩の順に多く，上位10部位では頭部（頭痛）を除くとすべてを，脊柱，関節など運動器関連の部位が占めている（**図1**）[6]．

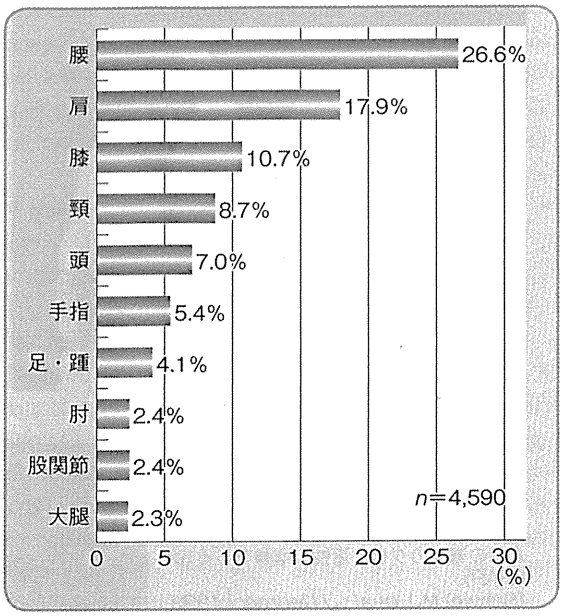

図1 慢性疼痛で最も困っている部位
（松平　浩他：ペインクリニック 2011；32：1345-1356より引用）

Nakamuraら[8]は，18歳以上の日本人の15.4%が運動器の慢性疼痛を有していると報告している（本誌S54ページ「日本における運動器慢性疼痛の疫学調査」参照）．

慢性疼痛の背景因子

Johannesら[1]は，低収入や失業などの社会経済的要因は，有意に慢性疼痛に関連していると報告している．また，離婚歴との関連性を認めたが，教育レベルとの関連性は否定している．一方，Landmarkら[3]は，低収入のほかに，低い教育レベル，高いBMIを慢性疼痛との関連因子として挙げている．わが国においては，このような慢性疼痛の背景因

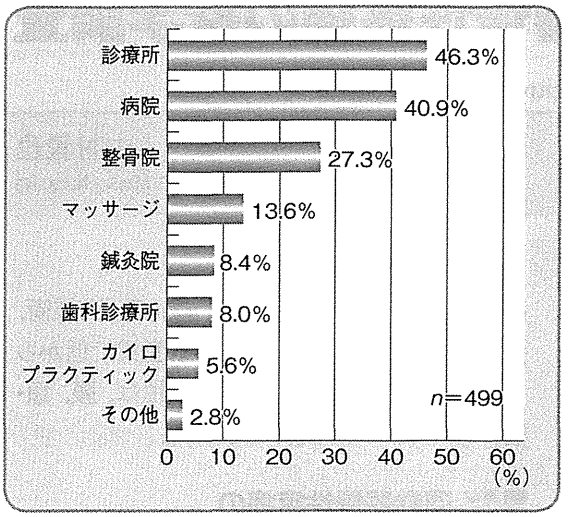

図2 慢性疼痛で受診した医療機関
(松平　浩他：日本における慢性疼痛の実態 ペインクリニック 2011；32：1345-1356より引用)

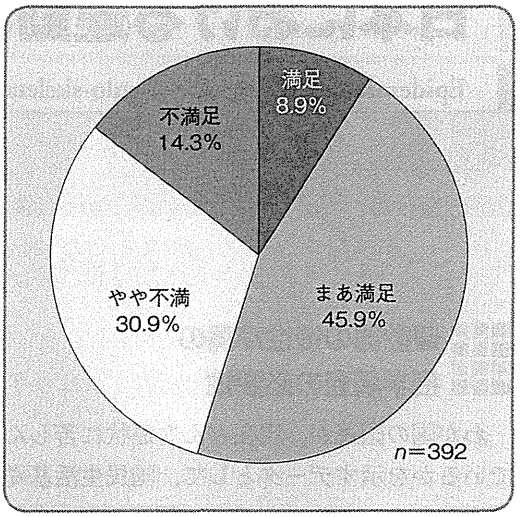

図3 慢性疼痛で診療所・病院を受診した患者の治療満足度
(松平　浩他：日本における慢性疼痛の実態 ペインクリニック 2011；32：1345-1356より引用)

子については十分明らかにされていない.

慢性疼痛治療の実態

松平ら[6]の調査では，慢性疼痛のために過去1年間に医療機関を受診した人は55.9%にとどまっていた．矢吹ら[7]の調査でも，57.5%が自己対処法，54.1%が情報収集，39.1%が薬剤購入などで対処したと回答(重複回答含む)している.

受診した医療機関の内訳では，診療所，病院の順に多いものの，整骨院，マッサージ，鍼灸院などのいわゆる代替医療の受診者が決して少なくないことが示されている(図2)[6]．診療所，病院の診療科では，整形外科が70～80%と格段に多く，内科が約20%で続く.

一方，診療所，病院を受診した人の治療満足度に関しては，松平ら[6]の調査では約45%が「やや不満」，「不満足」と回答しており，矢吹ら[7]の調査でも約70%が「満足のいく程度に痛みが緩和できていない」と答えるなど，慢性疼痛治療の難しさを浮き彫りにしている(図3).

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INDEX 学術

運動器の慢性疼痛

札幌医科大学リハビリテーション医学講座　村　上　孝　徳

はじめに

2011年、厚生労働省慢性の痛み対策研究班により本邦における運動器の慢性疼痛に関する調査が行われた。その結果15.4%に運動器慢性疼痛が存在するとの報告がなされた[1]。

運動器の慢性疼痛に限らず、疼痛性疾患を治療するに当たり目の前の疼痛がどのような病態にあるのかを理解することは治療の選択にあたり重要である。

運動器と疼痛

運動器は身体を支え、筋肉・関節の協調・分離的な働きによって随意的な行動を行う器官であり、日常生活を送るために不可欠な器官である。痛みは外傷、炎症などのトラブルを報せるシグナルであるとともに、痛み刺激は運動器に対し筋力低下、筋委縮、関節運動制限、筋痙縮・スパズム、浮腫を惹起し、効果的な働きを阻害する大きな要因となる。

疼痛概念

侵害受容性疼痛：侵害受容性疼痛（nociceptive pain）は熱刺激、機械的刺激あるいは化学的刺激などの侵害刺激によって侵害受容器が興奮することにより生ずる疼痛を指す。もっとも一般名的な概念で外傷や炎症などによる痛みが相当する。

神経障害性疼痛：神経障害性疼痛（neuropathic pain）は痛みの範囲が神経解剖学的に妥当かつ体性感覚系の損傷あるいは疾患の可能性があるものと定義される。絞扼性神経障害や椎間板ヘルニア・脊柱管狭窄症による神経根障害、帯状疱疹後神経痛などが相当する[2]。

疼痛性障害：いわゆる心因性疼痛と同義と考えてよい疼痛概念である。

感作性神経障害性疼痛

神経組織が明確な原因を指摘できない何らかの感作により機能異常をきたしているために生ずる疼痛を感作性神経障害性疼痛という概念で考えている。感作性神経障害性疼痛は有効な検査法がなく患者の症状、詳細な理学所見から想定されるものである（図1）。

慢性疼痛の概念

一般に慢性疼痛は「治療に要すると期待される時間枠組を超えて持続する痛みあるいは進行性の非癌性疾患による痛み」という2007年の国際疼痛学会による定義が用いられる。さらに国際疼痛学会では慢性疼痛の病態には侵害受容性疼痛、神経障害性疼痛、疼痛性障害が複雑に混在しているとしている。すなわち、慢性疼痛とは単一の疾病概念を表す用語ではないことに注

図1　疼痛病態の概念図

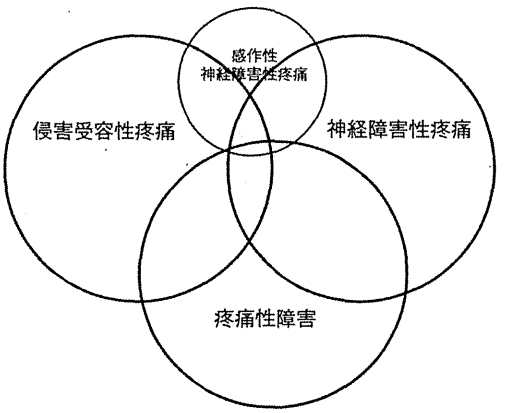
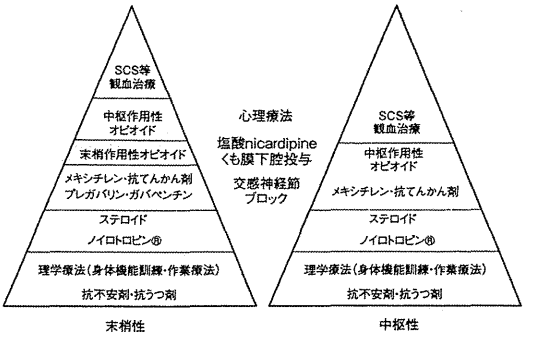


表1　国際疼痛学会による神経障害性疼痛治療ガイドライン

第一選択薬	Ca^{2+}チャネル$\alpha_2\delta$リガンド 三環系抗うつ薬(2級アミン) (2級アミンが無効時に3級アミンを使用) SNRI(セロトニン・ノルアドレナリン再取り込み阻害薬) 局所用リドカイン
第二選択薬	オピオイド トラマドール
第三選択薬	抗てんかん薬 抗うつ薬 メキシレチン NMDA(N-メチル-D-アスパラギン酸)受容体拮抗薬 カプサイシン

図2



意が必要である。

筆者は慢性疼痛の多くは感作性神経障害性疼痛が関与していると考えている。

感作性神経障害性疼痛に対する薬物療法

使用される薬剤はおおむね神経障害性疼痛に対する薬剤と同様である。処方にあたり留意している点は病態的に末梢性の疼痛なのか中枢性の疼痛なのかという疼痛の発生レベルを考慮することと複数の病態が関与している可能性を鑑み作用機序の異なる複数の薬剤を投与することである。さらに感作性神経障害性疼痛は経時的に病態が変化しうるため、初診時近傍の診断に固執しない態度も重要である。

神経障害性疼痛に対して国際疼痛学会、日本ペインクリニック学会からガイドラインが示されている（表1）[3,4]。我々は疼痛発生機序を考慮し、図2に示すような治療体系を試みている。

運動療法の重要性

運動療法は、正しい運動姿勢の獲得、筋力・持久力の増強、軟部組織のストレッチなどの介入により身体運動機能を高める治療である。

運動療法は患者の身体機能評価に基づき抗重力筋訓練、四肢筋力・関節可動域訓練などの基礎訓練、基本動作訓練から始める。さらに立位・歩行、屋内ADL訓練、交通機関の利用・職業動作訓練など社会生活を回復させる内容へ訓練対象を拡大していく。運動療法の担当分野は理学療法士が担うことが多いが運動機能の回復とともに実生活に即した合理的な動作を習得させる作業療法士の役割も大きい。具体的な動作の習得、ADL拡大は患者の励みとなりさらに復職等次のステップへ踏み出す能動的な意欲を育成する。この段階で可能であれば職業動作訓練など特異的な動作訓練をメニューに加えることでこの傾向を強化することができよう。この意味で運動療法は認知訓練、心理療法の要素をも含むといえる。

運動療法は具体的な課題をこなし、身体機能を増強することで二次的に痛みを軽減させることが期待できる。個々の運動機能へのアプローチは生活機能訓練へ結びつけるべきものであり、そのためには痛みの部位・程度のみならず、患者の心理状態・身体機能障害の程度・生活環境を把握しておく必要がある。

近年、慢性疼痛の治療法として認知行動療法（cognitive behavioral treatment）が注目されている[5]。認知行動療法はself-efficacyを高めることと要約することが可能である。認知行動療法は専門分野でのみなしえることではなく、運動機能訓練を通しても達成することが可能である。実施者が認知行動療法的な観点を念頭に置き運動メニューの策定、実施を行うことで患者の愁訴を積極的な痛みとの付き合い方に変換することが可能と考えている。

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ORIGINAL ARTICLE

Assessment of pain due to lumbar spine diseases using MR spectroscopy: a preliminary report

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Abstract
Background data There is a considerable difference in pain perception among individuals. In patients with chronic pain, recent studies using fMRI, PET and SPECT have shown that functional changes mainly occurred in the anterior cingulate cortex (ACC), prefrontal cortex (PFC) and thalamus. Brain magnetic resonance spectroscopy (MRS) can evaluate brain chemistry by measuring metabolites such as *N*-acetyl aspartate (NAA). The purpose of this study was to analyze whether brain MRS could assess pain due to lumbar spine diseases.
Methods NAA levels were determined relative to the concentration of creatine/phosphocreatine complex (Cr) and choline (Cho), which is commonly used as an internal standard. The NAA/Cr and NAA/Cho ratios in the ACC, PFC and thalamus were compared between six patients with unilateral pain (left side) and six control patients without pain.
Results In the right thalamus (contralateral side to symptom), the NAA/Cr in the patients with pain was statistically significantly lower compared with the control patients ($p < 0.05$). Also, in the right thalamus, the NAA/Cho in pain patients was significantly lower compared with controls ($p < 0.01$). When considering just the right thalamus, there were statistically significant correlations between the numerical rating scale for pain (NRS) and NAA values.
Conclusions Lumbar pain can be assessed indirectly by analyzing the decrease in NAA concentration in the thalamus.

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Introduction

Pain is one of the most frequent symptoms in lumbar spine diseases, as evaluated using a numerical rating scale (NRS), visual analog scale (VAS) and/or faces pain scale [1, 2]. However, there is a considerable difference in pain perception among individuals. Patients with lumbar spine diseases sometimes complain of severe pain that cannot be explained by physical findings or imaging studies. If pain is measured objectively, the pathogenesis of lumbar spine diseases and/or therapeutic efficacy may be evaluated more accurately. Thus, when considering that the pain pathway for objective pain measurement is ultimately recognized in the brain [3], cerebral imaging and/or metabolic studies can be useful.

Recent brain imaging such as functional MRI (fMRI) showed morphological and functional changes in the brain of patients with chronic pain [4–8]. Single-voxel proton magnetic resonance spectroscopy (MRS) is a non-invasive examination determining the cell metabolism of tissues and organs. A number of studies indicate that MRS can detect biochemical changes associated with functional brain abnormalities, such as epilepsy [9], dementia, Parkinson's disease, schizophrenia and depression [10]. Grachev and colleagues [11] have reported that in chronic low back pain (CLBP) patients, reductions in *N*-acetyl aspartate (NAA) and glucose were observed in the prefrontal cortex (PFC). Recently, Sharma and colleagues [12] showed that NAA levels in the primary somatosensory cortex decreased in patients with CLBP. Also, Gussew and colleagues [13]

demonstrated that reductions in NAA were observed in the anterior insula and anterior cingulated cortex in patients with non-specific CLBP.

CLBP pain is the most common cause of employees missing work for a long period [14]. It has been reported that CLBP is closely associated with depressive and anxiety states [15], and long-term LBP further exacerbates such psychiatric conditions [16]. When evaluating pain (LBP and sciatica) due to lumbar spine diseases using MRS, patients with a shorter duration of pain and without severe psychiatric conditions may be good candidates for analysis. The purpose of this study was to analyze whether MRS in these patients could assess pain due to lumbar spine diseases.

Subjects and methods

This study was approved by our institutional review board (no. 1254), and informed consent was obtained from each subject and control. Subjects studied included six patients complaining of unilateral pain (left side) due to lumbar spine diseases. The numerical rating scale (NRS) showed symptom severity was most painful during the day because pain became worse when moving and walking. Subject gender consisted of two males and four females. Age ranged from 28 to 68 years old (mean age 40 years). Diseases included two with disc herniation, three with spinal stenosis and one with idiopathic low back pain. Symptom duration was from 2 to 12 months (mean duration 5.7 months). Six healthy subjects without pain were used for control (Table 1). There were no significant differences in gender and age between the patient and the control groups. The brief scale for psychiatric problems in orthopedic patients (BS-POP) for medical personnel was used for evaluating psychiatric states. Verification of reliability, validity and reproducibility of the BS-POP has already been confirmed [17].

All MRI and MRS studies were performed with a 3-T clinical imaging instrument (Achieva 3.0T, Philips, The Netherlands). High-resolution sagittal and axial views were used for identification of the anterior cingulated cortex (ACC), prefrontal cortex (PFC) and thalamus (Fig. 1). Proton localized spectra were collected using point-resolved spectroscopy (PRESS). The settings for taking MRS were TR 2000 ms, TE 36 ms, voxel size 20 mm × 15 mm × 15 mm and NSA [number of sample (signals) averaged] 128. In the current study, we focused on *N*-acetyl aspartate (NAA) (Fig. 2). The value of NAA was measured relative to the concentration of the creatine/phosphocreatine complex (Cr) and choline (Cho), which is commonly used as an internal standard [4]. The NAA/Cr and NAA/Cho ratios in the ACC, PFC and thalamus were compared between the subjects and the controls. In all subjects, MRS was taken before treatment with medication or neuronal blocks.

Statistical analysis

Data were expressed as the mean ± SD. A non-parametric test (Mann-Whitney *U* test) was used for comparison among groups. Pearson's correlation coefficients were used to analyze the correlations between NRS and NAA values. p values <0.05 were considered statistically significant difference.

Table 1 Summary of subjects

Subjects or control	Age	Gender	Diagnosis	Symptom	NRS of pain	Duration of pain (months)	BS-POP
Subject 1	68	Female	LCS	Lt. sciatica	7	12	8
Subject 2	38	Female	LDH	Lt. LBP and sciatica	6	2	10
Subject 3	38	Female	LCS	Lt. sciatica	3	8	9
Subject 4	34	Male	LDH	Lt. sciatica	7	3	10
Subject 5	28	Male	Discopathy	Lt. LBP	8	2	11
Subject 6	34	Female	LCS	Lt. LBP and sciatica	4	7	8
Control 1	52	Male	–	–	0	–	–
Control 2	56	Male	–	–	0	–	–
Control 3	24	Male	–	–	0	–	–
Control 4	23	Female	–	–	0	–	–
Control 5	27	Male	–	–	0	–	–
Control 6	69	Female	–	–	0	–	–

LCS lumbar canal stenosis, *LDH* lumbar disc herniation, *LBP* low back pain, *NRS* numerical rating scale for pain, *BS-POP* brief scale for psychiatric problems in orthopedic patients