epidemiological research.[32]

LBP with disability was chosen as the outcome of interest to explore risk factors for new-onset LBP in the present study, as the assessment of severe LBP was considered more critical to both individuals and society in terms of health, workplace productivity, and healthcare cost. Although absence from work is often used as outcome measurement for disability in Western countries, disabling LBP in the current study was defined as LBP that interfered with work, regardless of sick leave. This was because the number of participants who took sick-leave due to disability was relatively small and both groups of people either absent or not absent from work shared similar median ODI values (data not shown). Our international epidemiological study previously showed that a sick-leave attributed to musculoskeletal disorders, predominantly LBP, appears to be much less common among Japanese workers than British workers.[33] The lower percentage of Japanese workers taking sick-leave due to disability compared to European countries may be a result of cultural differences towards one's work. Adding together both proportion of people leading and not leading to sick-leave in Japanese workers with disability was in turn almost equal to the proportion of those on sickness absence in UK. Therefore, when assessing Japanese workers, it seems reasonable to define LBP disability as LBP with work interference, with or without sick-leave.

The present study focused on LBP incidence among participants who were symptom free during the preceding year. Studies suggest that LBP is commonly recurrent.[5–8] Indeed, reported rates of recurrence in the first year after the episode vary between 24% and 87%.[34–38] Due to the high recurrence rate, the required duration of a symptom-free period for entry into research studies is typically between 1 to 3 months.[39] However, we sought to determine whether previous episodes of LBP would remain a predictor of future back pain even when subjects were symptom-free for at least a year. In this study, 3.9% of the participants had a new incident of disabling LBP during the 2 years of follow-up. The relatively low incidence of LBP in the current study may be a result of the strict definition of LBP disability as well as the requirement of a 1-year symptom-free period at study entry.

Our study results showed that previous episodes of LBP significantly increased the risk of a new episode of LBP disability, despite being symptom-free for more than one year. As previously reported,[40] frequent lifting was also a significant potential risk factor for LBP. Of the incident cases, 74.1% were of sudden onset, suggesting that the major cause of disability could be injury. Lifting tasks appeared to be reasonable for the risk of new-onset because physical movements may lead to injury. In contrast, in agreement with other studies,[41,42] a sedentary lifestyle was not associated with LBP disability. In this analysis, psychosocial factors, such as monotonous work and stress of interpersonal relations in the workplace, predicted risk of LBP after controlling for other variables. Another epidemiological survey also demonstrated that future LBP was strongly associated with stressful and monotonous work.[30] Although it is not intuitively understandable why work-related stress is a cause of LBP, biomechanical research suggests that psychological stress can contribute to an increased spinal loading and ultimately can increase the risk of injury.[31]

Although only four factors were chosen for the final multivariate analysis according to the predefined selection criteria, other factors also showed a trend for association with LBP. For example, frequent bending showed a notable effect on risk of LBP in univariate analysis. However, bending was highly correlated with lifting (rho=0.51). Due to collinearity, only one of these factors could be included in the multivariate model. In this case, lifting was chosen because ergonomic solutions could be more readily provided for lifting tasks. Moreover, a number of psychosocial factors, including job control, job fitness, vigor, and anxiety, nearly satisfied the criteria for entry into multivariate analysis. A post-hoc analysis was performed by stepwise selection of these variables along with the other significant factors. Ultimately, only the same four factors, selected based on the predefined procedures, remained in the final model (data not shown).

Unexpectedly, our findings appeared similar to those in Western countries. Initially, due to cultural differences, we expected that some potential risk factors would probably be different from elsewhere. The Westernization of Japanese culture may be reflected in the results of this analysis. Otherwise, the questionnaire may have simply not included factors that would have shown potential differences from other countries or cultures. Further investigation will be required to provide more precise reasons.

Limitations of this study warrant mention. First, the generalizability of findings is limited due to the sample included. For instance, the proportion of female participants was too small to be considered a representative sample of the total workforce, suggesting that the findings be treated with caution. Additionally, since the study was designed to recruit currently working people, those who had left the workforce due to LBP were excluded from the analysis, thereby potentially leading to an underestimation of disabling LBP. Another concern is selective drop-out. Of 5,310 participants, 3,914 were followed up on and entered into the analysis. This may introduce bias into the data analysis. To assess the effect of the selective drop-out, the baseline characteristics of participants who were followed up on and those who dropped out are calculated. The mean (SD) age was 43.4 (10.1) years and 38.5 (10.2) years, respectively, and the majority were male in both groups (80.7% vs 82.3%). Those who completed the study had mean (SD) BMI of 23.1 (3.2) while the values for dropouts were 23.0 (4.0). In the follow-up group (vs the drop-out group), 69.9% (vs 62.1%) were categorized as not manually handling any objects in their work, while 9.5% (vs 13.2%) were manually handling <20kg objects, 16.9% (vs 19.7%) were manually handling ≥20kg objects or were working as a caregiver, and 3.7% (vs 5.0)% were missing data. In both groups, the most common occupational fields in the categories of non-manual handling of objects, the manual handling of <20kg objects, and the manual handling of ≥20kg objects or working as a caregiver were desk work, manufacturing/ engineering and nursing, respectively. We considered that the baseline characteristics of both groups appeared to be not much different. Second, due to the nature of a self-assessment survey, some degree of misclassification is inevitable. Ideally, physical workload should be assessed by means of objective measures. Moreover, the survey questionnaire contained retrospective questions, so the possibility for recall bias should be kept in mind. Third, although the cognitive and emotional aspects of backache are known to have an effect on developing serious disability,[43] some important factors (e.g. fear-avoidance belief) were not evaluated in this study because appropriate questionnaires were not available in Japanese. Future studies should include self-report outcome measures, such as the Fear-Avoidance Belief Questionnaire (FABQ)[44] or the Tampa Scale of Kinesiophobia (TSK)[45,46] to assess the impact of these factors in Japanese workers. The Japanese versions of these questionnaires are now being developed. Lastly, the strategy of pre-selection for potential risk factors was not absolute. Although sex and age, which are known as well-established confounders, were included into the model, a more complicated model could explain the data better. Further assessment may help confirm these findings and find other potential risk factors.

In conclusion, our results suggest that ergonomic as well as psychosocial factors play a significant role in the development of future back pain disability after more than 1-year symptom-free period among Japanese workers. Previous studies have shown that a merely ergonomic intervention is not effective in preventing LBP.[9] Thus, both ergonomic and psychosocial factors should be addressed in workplace strategies aimed at preventing the new onset of LBP disability.

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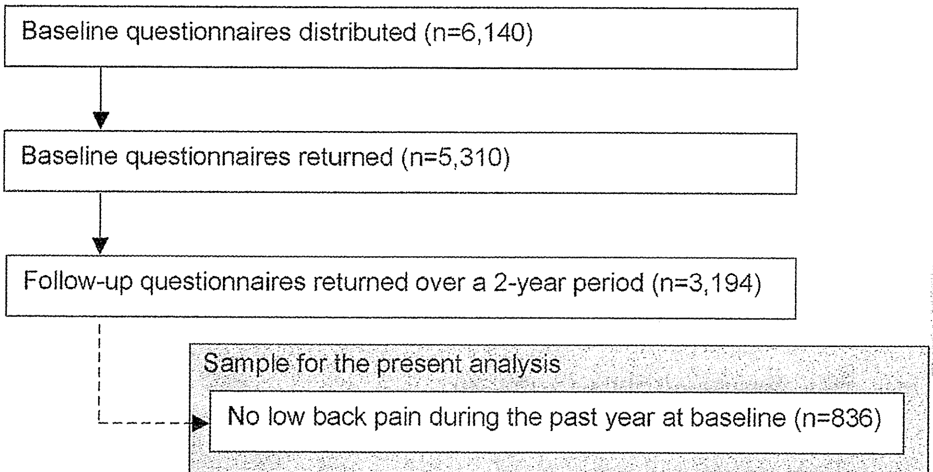

Table 1. Crude and adjusted odds ratios of baseline factors for the new onset of low back pain with work disability

Factors	%	Crude OR	95%CI	Adjusted OR	95%CI
Age (Years)					
< 40	35.5	1.00			
40-49	29.4	1.36	0.57-3.26		
≥ 50	35.1	1.27	0.54-2.99		
Gender					
Male	88.4	1.00			
Female	11.6	0.79	0.24-2.65		
Previous episodes of LBP					
No	59.8	1.00			
Yes	40.2	3.12	1.49-6.54		
Obesity[a]					
< BMI 25 kg/m^2	77.3	1.00		1.00	
≥ BMI 25 kg/m^2 (obesity)	22.7	0.96	0.41-2.25	0.92	0.38-2.18
Smoking habits[b]					
Non-heavy smoker	70.3	1.00		1.00	
Heavy smoker	29.7	1.55	0.74-3.25	1.43	0.62-3.28
Education					
College/University	71.5	1.00		1.00	
High school/Junior high school	28.5	1.07	0.48-2.37	1.08	0.47-2.45
Exercise habits					
≥ Once per week	36.4	1.00		1.00	
< Once per week	63.6	1.09	0.52-2.30	1.22	0.57-2.61
Flexibility[c]					
Flexibility	76.9	1.00		1.00	

Factors	%	Crude OR	95%CI	Adjusted OR	95%CI
Not flexible	23.1	0.79	0.32-1.97	0.78	0.31-1.95
Experience of current job					
< 5 years	31.3	1.00		1.00	
≥ 5 years	68.7	1.43	0.64-3.22	1.40	0.62-3.17
Working hours per week [d]					
< 60 hours	86.0	1.00		1.00	
≥ 60 hours	14.0	1.08	0.41-2.86	1.10	0.41-2.98
Work shift					
Daytime shift	86.4	1.00		1.00	
Nighttime shift	13.6	2.05	0.90-4.66	2.18	0.94-5.10
Employment status					
Full-time worker	95.4	1.00		1.00	
Other workers	4.6	1.35	0.31-5.87	1.34	0.29-6.19
Manual handling at work					
No manual handling (Desk work)	78.5	1.00		1.00	
Manual handling of < 20-kg objects	10.3	1.35	0.45-3.99	1.36	0.45-4.11
Manual handling of ≥ 20-kg objects or working as a caregiver	11.2	1.25	0.42-3.69	1.26	0.40-3.92
Bending [e]					
Not frequent	94.8	1.00		1.00	
Frequent	5.2	2.82	0.94-8.44	3.15	1.02-9.75
Twisting [e]					
Not frequent	97.1	1.00		1.00	
Frequent	2.9	2.30	0.52-10.27	2.59	0.56-12.05
Lifting [e]					
Not frequent	95.7	1.00		1.00	
Frequent	4.3	3.29	1.09-9.94	4.22	1.32-13.50
Hours of desk work [f]					
<6 hours per day	45.7	1.00		1.00	
≥ 6 hours per day	54.3	0.64	0.31-1.30	0.63	0.30-1.28
Mental workload (quantitative aspect) [g]					
No stress	58.3	1.00		1.00	
Stress	41.7	0.89	0.44-1.82	0.85	0.41-1.78
Mental workload (qualitative aspect) [g]					
No stress	59.3	1.00		1.00	
Stress	40.8	1.58	0.79-3.18	1.58	0.78-3.22
Physical workload [g]					
No stress	71.2	1.00		1.00	
Stress	28.9	1.44	0.70-2.98	1.71	0.81-3.61

Factors	%	Crude OR	95%CI	Adjusted OR	95%CI
Interpersonal stress at work [g]					
No stress	83.7	1.00		1.00	
Stress	16.3	2.42	1.12-5.21	2.60	1.18-5.75
Work environmental stress [g]					
No stress	79.1	1.00		1.00	
Stress	20.9	0.69	0.26-1.81	0.69	0.26-1.84
Job control [g]					
Controlled	86.0	1.00		1.00	
Not controlled	14.1	2.03	0.89-4.62	2.20	0.94-5.11
Utilization of skills and expertise [g]					
Utilization of skills and expertise	84.3	1.00		1.00	
No utilization of skills and expertise	15.7	1.78	0.78-4.03	1.91	0.82-4.43
Job fitness [g]					
Feeling fit	79.4	1.00		1.00	
Not feeling fit	20.7	1.99	0.95-4.20	1.98	0.93-4.21
Job satisfaction [g]					
Satisfied	80.8	1.00		1.00	
Not satisfied	19.2	1.59	0.73-3.50	1.59	0.72-3.54
Vigor [g]					
Vigorous	89.1	1.00		1.00	
Not vigorous	10.9	2.27	0.95-5.38	2.23	0.92-5.39
Anger [g]					
Not angry	76.1	1.00		1.00	
Angry	23.9	1.62	0.77-3.41	1.64	0.76-3.54
Fatigue [g]					
Not fatigue	78.3	1.00		1.00	
Fatigue	21.7	0.63	0.24-1.65	0.63	0.23-1.69
Anxiety [g]					
Not anxious	82.6	1.00		1.00	
Anxious	17.4	2.13	0.99-4.58	2.06	0.94-4.51
Depressed mood [g]					
Not feeling depressed	76.7	1.00		1.00	
Depressed	23.3	1.07	0.47-2.41	1.01	0.44-2.31
Somatic symptoms [g]					
No somatic symptoms	87.8	1.00		1.00	
Somatic symptoms	12.2	0.74	0.22-2.47	0.59	0.18-2.01
Support by supervisors [g]					
Support	77.4	1.00		1.00	
No support	22.6	1.60	0.74-3.45	1.50	0.69-3.25
Support by coworkers [g]					
Support	66.5	1.00		1.00	
No support	33.5	0.90	0.42-1.92	0.93	0.43-2.01

Factors	%	Crude OR	95%CI	Adjusted OR	95%CI
Support by family or friends [g]					
Support	83.4	1.00		1.00	
No support	16.7	1.16	0.47-2.87	1.11	0.44-2.81
Daily-life satisfaction [g]					
Satisfied	76.8	1.00		1.00	
Not satisfied	23.2	1.70	0.81-3.57	1.80	0.84-3.84
Monotonous work [h]					
Not monotonous	83.9	1.00		1.00	
Monotonous	16.1	2.34	1.09-5.05	2.58	1.18-5.64
Family history of LBP with disability					
No LBP with disability	85.8	1.00		1.00	
LBP with disability	14.2	1.78	0.75-4.23	1.75	0.73-4.21

OR: Odds ratio, CI: Confidence interval, BMI: body mass index, LBP: low back pain

Adjusted for age, gender, and previous episodes of low back pain.

[a] Obesity: BMI of ≥25 is defined as obesity in Japan.

[b] Smoking habits: Brinkmann index, calculated from the total number of cigarettes smoked per day multiplied by duration of smoking in years, of ≥400 was defined as heavy smoker.[27]

[c] Flexibility: flexibility was determined if wrists could reach beyond the knees, but fingertips could not reach the ankles.[28]

[d] Working hours: ≥ 60 hours per week of uncontrolled overtime.

[e] Bending, twisting, lifting: ≥half of the day as frequent.

[f] Hours of desk work: longer than 6 hours was determined as static posture.

[g] Work-related stress factors assessed with the brief job stress questionnaire: not feeling stressed, feeling stressed: the 5 original responses were reclassified into "not feeling stressed", where low, slightly low and moderate were combined, and "feeling stressed", where slightly high and high were combined.

[h] Monotonous task: feelings of monotony or boredom at work.

Table 2. Multivariate-adjusted odds ratios for the new onset of low back pain with work disability

Factors	Adjusted OR[a]	95%CI
Previous episodes of low back pain		
No	1.00	
Yes	3.25	1.53-6.91
Lifting		
Not frequent	1.00	
Frequent	3.77	1.16-12.3
Monotonous work		
Not monotonous	1.00	
Monotonous	2.21	0.99-4.94
Interpersonal stress at work		
No stress	1.00	
Stress	2.42	1.08-5.43

OR: Odds ratio, CI: Confidence interval

[a] Adjusted for previous episodes of low back pain, lifting, monotonous work, interpersonal stress at work, age and gender.

特集 リウマチ性疾患の痛みをやさしく教えます

運動器疾患における神経障害性疼痛

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Key Words ▶▶▶▶ 神経障害性疼痛 中枢性感作 変形性関節症 後縦靱帯骨化症 プレガバリン

神経障害性疼痛は国際疼痛学会で「体性感覚系に対する損傷や疾患の直接的結果として生じている疼痛」と定義され，痛覚過敏やアロディニアを特徴とする非ステロイド性抗炎症薬抵抗性の痛みである．神経根症など脊椎疾患の多くにみられ，四肢運動器の障害においても生じている可能性がある．

はじめに―神経障害性疼痛とは？―

現在，痛みは①侵害受容性疼痛，②神経障害性疼痛，③心因性疼痛（または機能性疼痛）に分類される．①の侵害受容性疼痛は，痛み情報が皮膚などの侵害受容器から脊髄後角を経て外側視床路を通る上向路を中心とした，生体へのさまざまな有害な外的侵襲に対する生理的反応である．また，③の心因性疼痛は身体表現性疼痛とほぼ同義で，身体の障害から予測される痛みをはるかに超える痛みがあり，心理的要因が原因の過半であると診断された場合に用いられる．

神経障害性疼痛は知覚神経の障害による痛みであり，痛覚過敏や通常は痛くない程度の刺激を痛みと感じるアロディニア，神経障害で妥当と思われる部位への電撃痛や刺すような痛み，焼けるような痛みなどを特徴とする．末梢から脊髄後角そして脳に至る感覚神経系のさまざまなレベルで生じると想定されており，国際疼痛学会（International Association for the Study of Pain：IASP）において「体性感覚系に対する損傷や疾患の直接的結果として生じている疼痛」[1]と定義されている．診断ではIASPから診断アルゴリズム[2]が提唱され，スクリーニングとして神経障害性疼痛用調査票が各国で作成されている．われわれはpainDETECT[3]を用いている．ただ，臨床上は侵害受容性疼痛と神経障害性疼痛が併発している場合が多い．また痛み刺激は内側脊髄視床路を通り前帯状回や扁桃体に至る痛みの情動系も賦活化するため，抑うつや不安といった情動障害が起こりやすい．すなわち，上記3種類の痛みはほとんどの臨床例でオーバーラップして表出されていることを認識する必要がある．治療の観点からは各種薬剤の効果が異なることが重要であり，侵害受容性疼痛では非ステロイド性抗炎症薬（non-steroidal anti-inflammatory drugs：NSAIDs）が比較的有効であるが，神経障害性疼痛ではNSAIDsの効果はきわめて限定的であり，抗けいれん薬や抗うつ薬が有効である．

神経障害性疼痛用調査票を用いた疫学調査では一般人の7～8％[4]に神経障害性疼痛がある．また，運動器疾患を担当する整形外科の慢性疼痛外来患者の39～43％[5]に

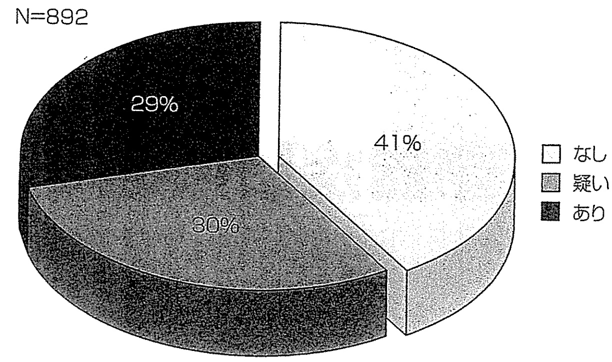
みられるとされる．外傷や腫瘍性疾患などでも神経障害性疼痛の関与はあると思われるが，本稿では脊椎と四肢変性疾患について触れる．

1．脊椎変性疾患における神経障害性疼痛

脊椎症において神経障害は以前から脊椎疾患の主たる課題である．ただし運動障害すなわち麻痺に大部分の関心が注がれてきた点は否めない．欧州の腰痛患者に対する調査では25〜30％に神経障害性疼痛の関与があると報告されている[9]．われわれが厚生労働省研究班でおこなった2010年の頸椎後縦靱帯骨化症に対する調査では神経障害性疼痛のある患者が29.8％を占め，疑いを含むと6割にみられた（図❶）．また2011年におこなった腰部脊柱管狭窄症に対する調査では神経障害性疼痛のある患者が13.8％，疑いを含むと5割にみられた．

神経障害性疼痛の代表としては腰椎椎間板ヘルニアにみられる腰部神経根症（根性坐骨神経痛）や変形性頸椎症に伴う頸部神経根症がある．いずれも強烈な痛みを起こしうる病態であり，即効的な疼痛緩和には大量ステロイドの短期内服やブロック治療が望ましい．より有害事象の少ない治療として2010年から使用可能となったプレガバリンがよい．ただし，めまいやふらつきが一時的に出現することが多いため，処方開始時からすぐに有効量を投与することはむずかしい．運動障害が高度あるいは進行する例や，上記保存治療で痛みを緩和できない場合には圧迫部位の解除すなわち除圧手術が必要である．プレガバリンはきわめて有効な場合があり，手術が回避できた例がしばしばある．

また，手術で圧迫を解除しても神経障害性疼痛が治癒しない場合も少なくない．われわれが2007年におこなった調査では脊椎手術を受けた患者においても2割程度の患者は日常生活に支障をきたすような痛みが残存していた[10]．また腰部脊柱管狭窄症後の足底部のしびれが残りやすいことが知られており，治療満足度にも影響する[11]．腰椎椎間板ヘルニアの術後にプレガバリンを投与すると残存する痛みが緩和され治療成績が向上した報告があり[12]，手術治療をおこなう患者でも神経障害性疼痛を意識して治療に臨む必要がある．



図❶　後縦靱帯骨化症の神経障害性疼痛

2．変形性関節症における神経障害性疼痛

四肢の変形性関節症（osteoarthritis：OA）における痛みの主体は何であろうか？変性は関節軟骨の変性，磨耗からはじまるとされているが，神経終末がないため正常軟骨に痛みが生じることはない．軟骨変性から軟骨下骨の障害，それに引きつづいて生じる骨棘形成や滑膜炎が原因とされる侵害受容性疼痛と考えられており，病期によっては炎症性疼痛が主体となる．しかし近年，侵害受容性疼痛と炎症性疼痛のみではなく，神経障害性疼痛の関与があることがしだいに明らかになってきた．関節組織が障害を受けると，マクロファージやリンパ球などから各種 nerve growth factor やサイトカインが放出され，神経終末の刺激に対する閾値を低下させる．こうした，いわゆる末梢性感作が脊髄後角にある痛み伝播を増幅させ修飾させると中枢性感作が生じ[6]，さらに痛みに病的に敏感な状態，すなわち神経障害性疼痛となる．高齢者の膝OAに対する調査票の研究では28％に神経障害性疼痛の要素があったとされる[7]．また，Caチャネル $\alpha_2\delta$ サブユニットをブロックするプレガバリンは三環系抗うつ薬とならんで神経障害性疼痛の第一選択薬であるが，人工膝関節手術の術後投与によって痛みが緩和され治療成績が向上したことがランダム比較試験で示されている[8]．このように神経障害性疼痛は四肢関節変性疾患においても重要な病態であると認識されはじめている．

おわりに

神経障害性疼痛の代表的な疾患は線維筋痛症や複合性

局所疼痛症候群，脊髄障害性疼痛症候群であるが，運動器疾患に広くみられる病態である可能性が高くなっている．今後，運動器疾患の診療においては神経障害性疼痛を念頭に置いてあたる必要があるだろう．

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