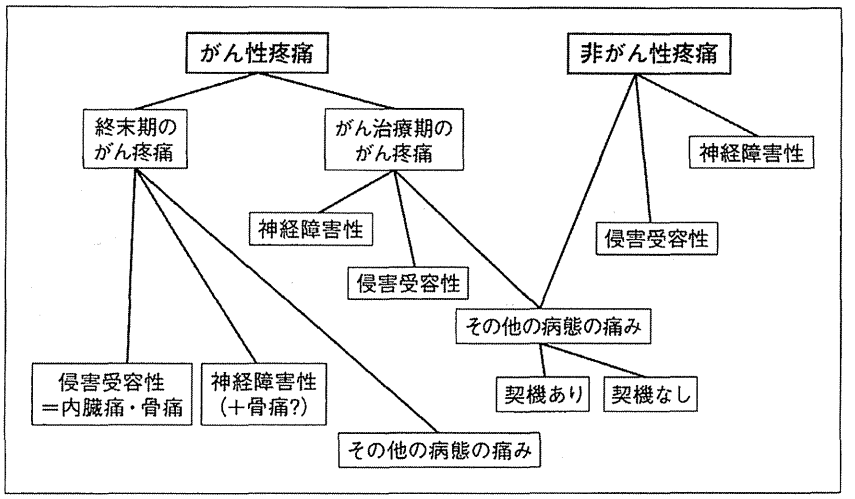

図 3　オピオイド鎮痛薬の適応を検討する際の病態とその分類

オピオイド鎮痛薬の適応を検討する場合には，まずがん性疼痛であるか非がん性疼痛であるかの判断をする．続いて，その病態に合わせた治療計画を検討する．原則的にオピオイド鎮痛薬の使用量はモルヒネ換算120 mg/dayを上限として設定し，頓用は行わない(トラマドールの上限である400 mg/dayはモルヒネ換算80 mg/dayである)．これはオピオイド鎮痛薬に対する精神依存から患者を保護するための措置である．

や末梢神経ニューロパチーの急性増悪などのように緊急性のある重症の神経障害性疼痛治療の際には，トラマドールおよび強オピオイド製剤を第3選択薬として用いるのではなく，第1選択薬のひとつとして考慮することが治療指針で推奨されている[8]．これはトラマドールなどの鎮痛効果が強力かつ速効性があり，鎮痛必要量に漸増させるまでの期間が比較的短いことが理由としてあげられている．

このほか，がん患者の生命予後の延長には十分な睡眠が必要[9]であることが知られているが，トラマドールによる疼痛管理は，日中の眠気が少なく夜間の睡眠の質が向上することが示されており，がん治療自体を支持する可能性が示唆されている．さらに，がん手術などによる侵襲はがん免疫をつかさどるnatural killer(NK)細胞活性を低下させるが，トラマドールによるがん術後鎮痛は先制鎮痛効果をもつほか，NK細胞活性の低下が抑制され，がん転移が少なくなることが基礎実験で示されており，がん治療自体への有用性も期待される[10,11]．

トラマドールカプセル剤は2012年9月にがん性疼痛だけでなく非がん性慢性疼痛に対しても適応が拡大され，多様な疼痛疾患に対して用いることができるようになっている．トラマドールの高い鎮痛効果と認容性に加え，十分な注意が必要ではあるが依存性発現の少なさと長期安全性から，がん治療期の患者と多くの非がん性慢性疼痛患者にとって有用であると考えられる(図3)．

おわりに

痛みはQOLの甚大な阻害因子である．トラマドールは侵害受容性疼痛と神経障害性疼痛に対するもっとも確実な鎮痛薬のひとつであり，疼痛患者のQOLは大きく改善する．国際疼痛学会は2010年の学術集会の際に第1回Pain Summitを併催し，モントリオール宣言[12]を採択した．そのなかでもオピオイド鎮痛薬が十分に患者に行き届いていない現状を憂慮する文面が記載されている．終末期がん性疼痛，がん治療期の疼痛，非がん性慢性疼痛を問わず，オピオイド鎮痛薬に対する“恐怖症”ともよぶべき安易な“不使用”は，患者のために是正されなければならない．

その一方で，アメリカでは患者の痛みの訴えのままに十分な患者評価と教育をせず，痛みとオピオイド鎮痛薬についての説明義務が果たされないままにオピオイド鎮痛薬が安易に大量に処方されてきた結果，全人口当り約0.3%(＝75万人)がオ

ピオイド鎮痛薬に対する嗜癖と精神依存を発症しているという衝撃的な報告もある[13]．わが国ではアメリカを反面教師として，このような状況を生み出さないためにも，依存性発現が少なく長期使用の安全性が比較的高いオピオイド鎮痛薬，すなわちトラマドールを基軸として，オピオイド鎮痛薬の利点と欠点を十分に理解したうえで適切に使用し，患者利益に供するとともに社会秩序の維持がはかられなければならない．

モントリオール宣言「疼痛治療を受けることは基本的人権である(Access to pain management is a fundamental human right)」は，単純に痛みを寛解させることだけを謳っているわけではなく，これは安易なオピオイド鎮痛薬の処方に対する牽制を暗に示しているとわれわれは受け止めており，非がん性慢性疼痛に対する治療目標の設定は「痛みがあっても有意義な生活を獲得・維持すること」とする日本ペインクリニック学会治療指針の基本的概念に合致するものと考えられる．したがって，トラマドールを代表とするオピオイド鎮痛薬を用いて患者のQOLを改善することとともに，オピオイド鎮痛薬に対する精神依存の形成から患者を保護することは医師の責務であり，オピオイド鎮痛薬の適正使用が懸念される患者に対してオピオイド鎮痛薬を処方しないことは医師の権利である．

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文献/URL

1) Thienthong, S. et al.：*J. Med. Assoc. Thai.*, **89**：1120-1126, 2006.
2) Maltoni, M. et al.：*Support Care Cancer*, **13**：888-894, 2005.
3) Temel, J. S. et al.：*N. Engl. J. Med.*, **363**：733-742, 2010.
4) Bandieri, E. et al.：*Ann. Oncol.*, **23**：2016-2020, 2012.
5) Grond, S. and Sablotzki, A.：*Clin. Phramacokinet.*, **43**：879-923, 2004.
6) Leppert, W. and Luczak, J.：*Support Care Cancer*, **13**：5-17, 2005.
7) Allen, S. C.：*Oncology*, **74**：S76-S82, 2008.
8) Dworking, R. H. et al.：*Pain*, **132**：237-251, 2007.
9) Mormont, M. C. et al.：*Clin. Cancer Res.*, **6**：3038-3045, 2000.
10) Gaspani, L. et al.：*J. Neuroimmunol.*, **129**：18-24, 2002.
11) Sacerdote, P. et al.：*Anesth. Analg.*, **90**：1411-1414, 2000.
12) IASP. http://www.iasp-pain.org/AM/Template.cfm?Section=Declaration_of_Montrand Num233_al
13) http://www.samhsa.gov/data/NSDUH/2k10NSDUH/2k10Results.htm

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5．オピオイド鎮痛薬の薬物相互作用

1）トラマドールの薬物相互作用

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運動器疼痛メディカルリサーチ&マネジメント

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5．オピオイド鎮痛薬の薬物相互作用

1）トラマドールの薬物相互作用

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運動器疼痛メディカルリサーチ&マネジメント

要　旨

トラマドールはμオピオイド受容体完全作動作用とセロトニン・ノルアドレナリン再取り込み阻害（SNRI）作用が相乗的に働いて鎮痛効果を発揮し，侵害受容性疼痛と神経障害性疼痛のいずれにも有効で，オピオイド鎮痛薬に対する精神依存の形成も少ない．しかし，この2つの鎮痛機序から薬物相互作用についても2つの視点が必要であるだけでなく，トラマドールが肝臓での代謝を受けて産生される代謝産物が活性を持つことも薬物相互作用の面で理解が必要である．

（ペインクリニック 35：S398-S406，2014）

キーワード：オピオイド鎮痛薬，オピオイド受容体作動作用，
セロトニン・ノルアドレナリン再取り込み阻害作用

はじめに

トラマドールは一般にオピオイド鎮痛薬に分類されるが，その化学構造にはオピオイド骨格だけでなくモノアミン骨格が含まれ，鎮痛作用はオピオイド受容体作動作用だけでなくセロトニン・ノルアドレナリ再取り込み阻害作用によっても発揮される（**図1**）．トラマドールのオピオイド骨格のμ，δ，κオピオイド受容体に対する親和性（Ki 値）はモルヒネに比して非常に低く，トラマドールのオピオイド骨格のモノアミンポンプに対する親和性は，三環系抗うつ薬のイミプラミンに比して非常に低い（**表1**）[1)]．したがって，トラマドールの鎮痛作用はμオピオイド受容体作動作用とセロトニン・ノルアドレナリン再取り込み阻害作用が相乗的に働いているものと考えられ，μオピオイド受容体拮抗薬であるナロキソンを投与してもトラマドールの鎮痛効果は完全に抑制されない[2)]．一方，トラマドールに比してトラマドールの代謝産物である M1 はμオピオイド受容体に対する親和性が相対的にかなり高い．トラマドールは弱オピオイドに位置づけられるものの，ペンタゾシンやブプレノルフィンなどの他の弱オピオイド鎮痛薬と異なり，トラマドールとその代謝産物はμオピオイド受容体に対して完全作動薬として働くため，侵害受容性疼痛に対する鎮痛作用に天井効果がなく，用量依存性に鎮痛効果が発揮される（**図2**）．

Drug interaction of tramadol
Masahiko Sumitani, et al
Department of Palliative Care/Anesthesiology and Pain Center, The Tokyo University Hospital

表1　トラマドールの各種受容体に対する親和性（文献1より引用改変）

化合物	親和性　Ki（μM）				
	オピオイド受容体			ノルアドレナリン再取り込み阻害ポンプ	セロトニン再取り込み阻害ポンプ
	μ	δ	k		
トラマドール	2.1	57.6	42.7	0.78	0.99
活性代謝物 M1	0.0121	0.911	0.242	1.52	5.18
コデイン	0.2	5.1	6.0	(－)	(－)
モルヒネ	0.00034	0.092	0.57	(－)	(－)
イミプラミン	3.7	12.7	1.8	0.0066	0.021

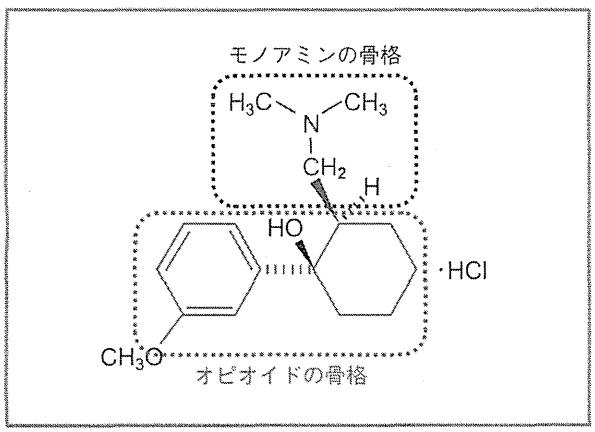

図1　トラマドールの化学構造式
トラマドールはオピオイド骨格とモノアミン骨格を持つ

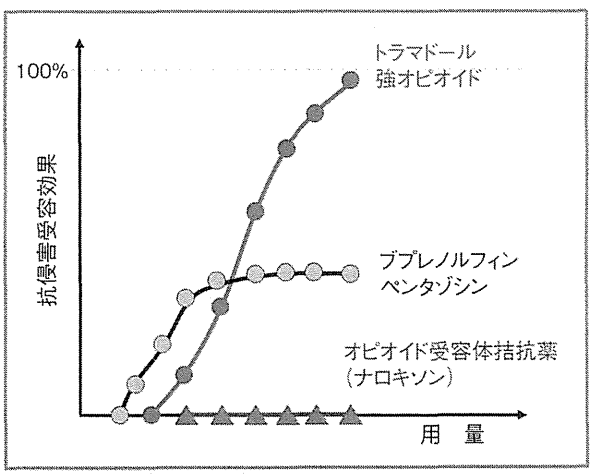

図2　各種オピオイド鎮痛薬の用量-反応曲線シェーマ
トラマドールと強オピオイド鎮痛薬はオピオイド受容体に対する完全作動薬であるため，用量依存性に抗侵害受容効果が確実に得られる．一方，ブプレノルフィンやペンタゾシンはオピオイド受容体部分作動薬であるため，抗侵害受容効果は頭打ち（天井効果）になる．また，オピオイド受容体拮抗薬であるナロキソンは抗侵害受容効果を持たない

1．疼痛下行性抑制系とその神経伝達物質

疼痛下行性抑制系に関わる神経伝達物質は，セロトニン，ノルアドレナリン，オピオイド，ドパミン，グルタミン酸，GABA，CCKなどが知られている．この中でも，脊髄後角の侵害受容神経細胞を直接的に抑制し，疼痛の上行性伝達を抑制する物質としては，ノルアドレナリンとセロトニンについての研究が最も進んでいる（図3）[3]．さらに，オピオイド鎮痛薬は，脊髄後角神経細胞を直接的に抑制するだけでなく，中脳水道周囲灰白質や延髄RVM核を興奮させ下行性抑制系を賦活させる間接的な鎮痛効果の方が強い．痛みの病態には侵害受容性疼痛と神経障害性疼痛が定義されているが，最近では，国際的にまだ議論の余地はあるものの，中枢機能障害性疼痛という新たな病態が提唱されており，その発症機序は疼痛下行性抑制系の機能減弱とされ，線維筋痛症や慢性腰痛，外傷性頸部症候群などのように，器質的組織障害や炎症所

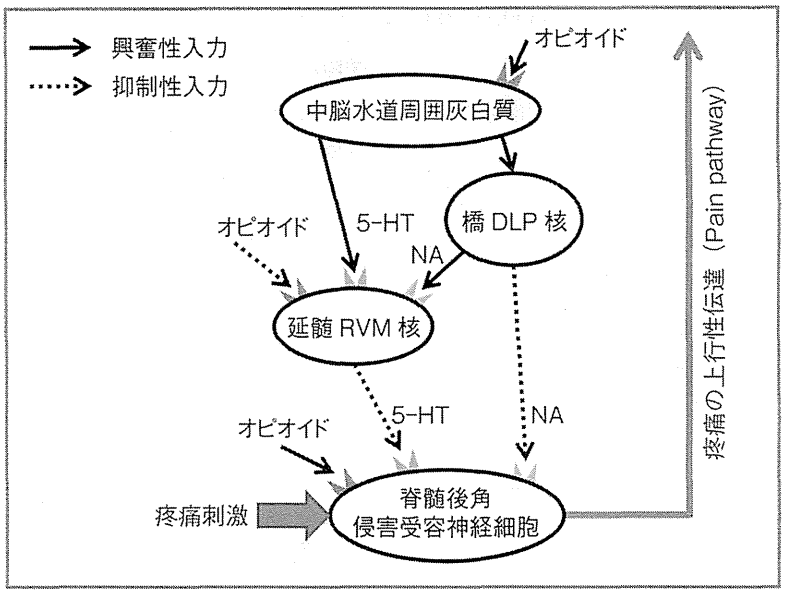

図３　疼痛下行性抑制系のシェーマ（文献３より引用改変）

見を伴わないにもかかわらず知覚される痛みのことを指す．中枢機能障害性疼痛は functional pain syndrome や functional somatic syndrome とも呼ばれ，精神情動的問題が主因とする心因性疼痛とは明らかに異なる概念である．加えて，神経障害性疼痛[4]や侵害受容性疼痛[5]でも疼痛下行性抑制系の機能が減弱することが基礎研究によって示されており，中枢機能障害性疼痛に進展していくことが考えられる（図４）．このような疼痛下行性抑制系の機能減弱を特徴とする中枢機能障害性疼痛の併存は，慢性膵炎や神経障害性疼痛，複合性局所疼痛症候群患者で臨床的にも支持されている．

２．強オピオイド鎮痛薬とトラマドールの相互作用

オピオイド鎮痛薬の慢性使用では，オピオイド鎮痛薬に対する耐性が形成され，鎮痛効果が減弱し，比較的高用量のオピオイド鎮痛薬が必要になることも珍しくない．マウスにモルヒネを慢性投与したモルヒネ耐性モデルでは，フェンタニルを投与しても鎮痛効果がほとんど得られないが，トラマドールの投与では理論的に予想される相加的な鎮痛効果を上回る高い鎮痛効果が得られる（図５）[6]．オピオイド鎮痛薬に対する耐性形成には，オピオイド受容体に関するものを含め様々なメカニズムが明らかにされているが，このような条件下でもトラマドールが高い鎮痛効果を発揮することができるのは，セロトニン・ノルアドレナリン再取り込み阻害作用による疼痛下行性抑制系の賦活によると考えられる．また，ペンタゾシンなどの他の弱オピオイド鎮痛薬とモルヒネの併用では，理論的に予想される相加的な鎮痛効果を下回る鎮痛効果しか得られず，これはトラマドール以外の弱オピオイド鎮痛薬がμオピオイド受容体に対して部分作動性あるいは拮抗性であることが原因であると考えられ，トラマドールがμオピオイド受容体に対する完全作動薬であることとの大きな違いである．さらに，間欠的寒冷刺激ストレスによる中枢機能障害性疼痛モデルマウスでは，全身性のアロディニアを呈し，オピオイド鎮痛薬に抵抗性である．このようなマウスでは，モルヒネ投与により髄液中のセロトニン代謝産物の濃度が低くなっており，疼痛下行性抑制系

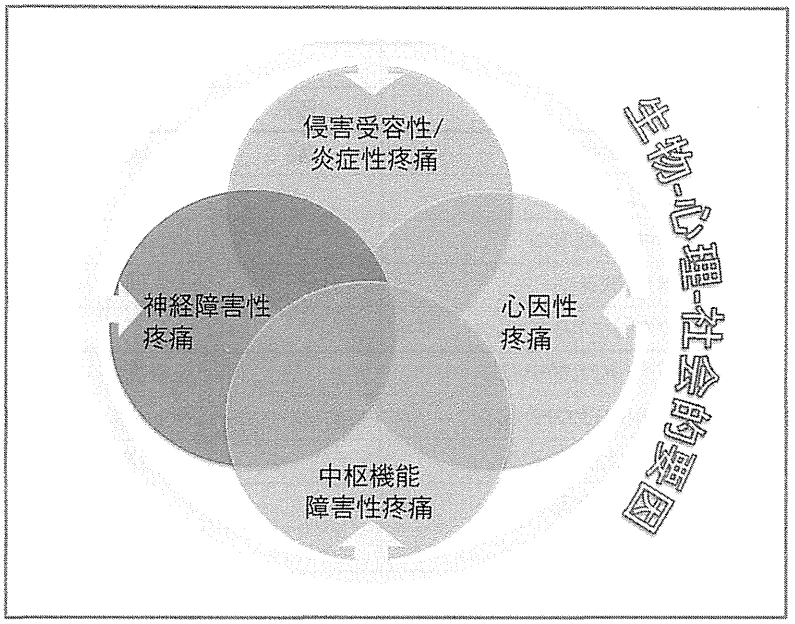

図4　痛みの病態
侵害受容性（炎症性）疼痛，神経障害性疼痛が器質的障害に起因する痛みであり，心因性疼痛と中枢機能障害性疼痛が非器質的な痛みである．これらの病態はオーバーラップする概念であり，これらを生物心理社会的要因が修飾する

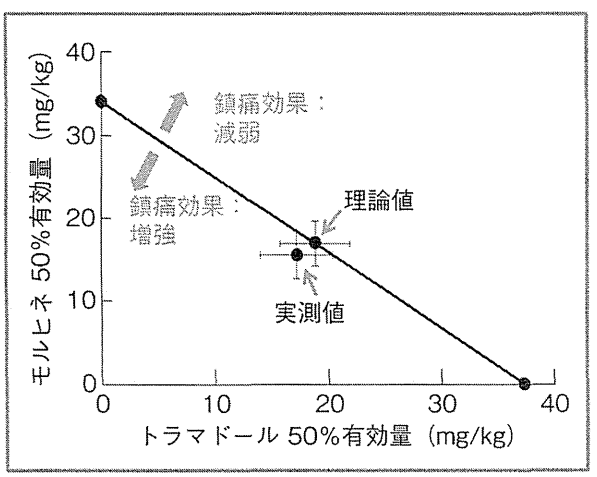

図5　トラマドールとモルヒネのアイソボログラフィック解析
トラマドールとモルヒネの併用は相加的な鎮痛作用の理論値よりも強い鎮痛効果を発揮する

が機能していないことが示唆される[7]．侵害受容性疼痛と神経障害性疼痛のいずれでも痛みを慢性的に経験している患者の多くは，痛みというストレスを抱えて生活しているので，ストレス誘発性の中枢機能障害性疼痛の病態が併存し，オピオイド抵抗性が生じている可能性も考えられる．臨床的にある程度高用量の強オピオイド鎮痛薬を用いても疼痛コントロールが不良な重度変形性関節症患者に対して，トラマドール 200 mg/日を併用することによって，疼痛が著明に軽減し，QOL が改善することが示されており，基礎研究の結果が臨床的にも裏づけられている[8]．ただし，侵害受容性疼痛や神経障害性疼痛のように器質的な痛みがない状態では，オピオイド鎮痛薬に対する依存性が発現しやすいことが基礎研究によって示されており，器質的原因のない中枢機能障害性疼痛では，トラマドールの適応については十分に注意が必要である．

表2　各種薬物の代謝に関わるチトクローム P450 のサブタイプ（文献 14 より引用改変）

代謝される薬物		CYP サブタイプ		
		2B6	2D6	3A4
オピオイド鎮痛薬	トラマドール	高	低	高
	フェンタニル			高
	オキシコドン		低	高
	メサドン		低	高
	ブプレノルフィン			低
抗うつ薬	アミトリプチリン		高	低
	ノルトリプチリン		高	高
	クロミプラミン		高	高
	イミプラミン		高	高
	ミアンセリン		高	低
	フルボキサミン		高	
	マプロチリン		高	
	パロキセチン		高	
	セルトラリン		高	高
NSAIDs 他	セレコキシブ			低
	メロキシカム			低
	アセトアミノフェン			低
	デキストロメトルファン		低	高

トラマドールは主としてチトクローム P450 の 2B6，2D6，3A4 で代謝されるので，この 3 種だけに特化して示す

3．セロトニン受容体拮抗薬とトラマドールの相互作用

トラマドールの鎮痛効果は，オピオイド受容体作動作用以外に，セロトニン・ノルアドレナリン再取り込み阻害作用による．がん化学療法による悪心や嘔吐に対して用いられるオンダンセトロンなどのセロトニン受容体拮抗薬は，疼痛下行性抑制系の効果を減弱させるため，開腹術後の創部痛に対するトラマドールの鎮痛効果を減弱させ，患者自己調節鎮痛薬の必要量が増加することが示されている[9]．本邦でのトラマドールの内服薬は，当初，がん性疼痛に対して適応されており，長期使用によるオピオイド依存が生じにくいという臨床データ[10]からも，終末期だけでなくがん治療期での疼痛治療に対する有用性が期待されてきた．したがって，がん化学療法とそれに伴う嘔気対策としてオンダンセトロンなどのセロトニン受容体拮抗薬を使用している患者に対してトラマドールを使用する臨床場面は多いことが想定され，トラマドールの鎮痛効果の減弱が起こり得ることは認識されなければならない．ただし，疼痛下行性抑制系に関与するセロトニン受容体のサブタイプは 5-HT_{1B} と 5-HT_3 受容体が主として関与している[11]．一方，セロトニン拮抗薬による制吐作用は 5-HT_3 受容体を主として拮抗することによ

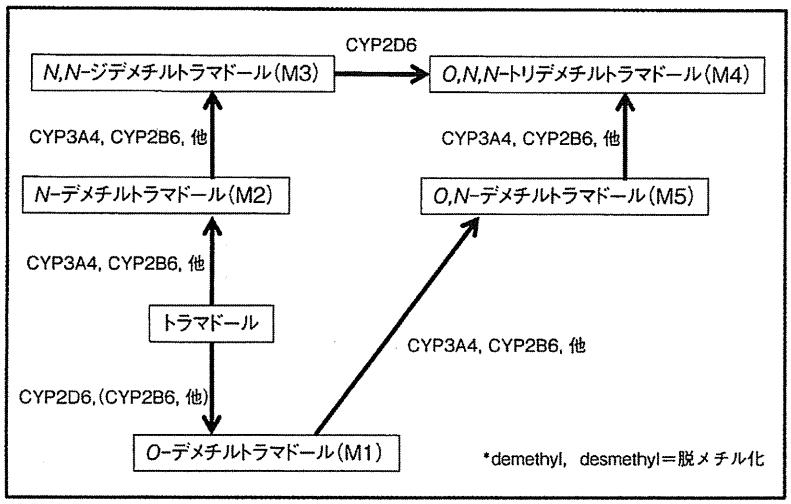

図6　トラマドールの代謝経路

る．したがって，トラマドールとセロトニン受容体拮抗薬の併用は鎮痛効果を減弱させると考えられる一方で，5-HT_{1B} 受容体の作用のためか，トラマドールと制吐剤のセロトニン受容体拮抗薬を併用しても鎮痛効果が減弱せず，また，制吐作用も減弱しないとする臨床データ[12]もあり，これらの併用が必ずしも注意を要するという訳ではない．ちなみに，疼痛下行性抑制系だけでなく，上位中枢から脊髄後角侵害受容神経細胞の興奮性を高める疼痛下行性促進系もわれわれの生体には備えられているが，疼痛促進系に関わるセロトニン受容体は主として 5-HT_{1A} であるためセロトニン受容体拮抗薬の使用による痛覚過敏の報告はなく，がん性疼痛を有するがん患者が化学療法を受ける際にセロトニン受容体拮抗薬を制吐剤として併用することに躊躇は不要である．

4．チトクローム P450 関連薬とトラマドールの相互作用

複数種類の薬物を併用した際の薬物動態学的な相互作用の多くは，代謝を介した相互作用であり，その 90%以上にチトクローム P450（cytochrome P450：CYP）が関与する．CYP が関わる相互作用はさらに酵素阻害と酵素誘導に基づくものに分類されている．

トラマドールは，他の多くのオピオイド鎮痛薬や抗うつ薬などと同様に，CYP による代謝を受ける（**表2**）[13]．CYP は様々なファミリーとサブファミリー，ポリペプチドによって分類されるが，トラマドールの薬物代謝に関わる CYP は，CYP2D6 と CYP3A4 と CYP2B6 の3種が最も重要である（**図6**）[14]．CYP2D6 はこの3種の中ではトラマドールの代謝自体への関与は比較的低いが，トラマドールを O-脱メチル化反応（demethylation, desmethylation）することによって，トラマドール自体よりもμオピオイド受容体への親和性が高い活性代謝産物である M1 を産生する代謝経路に関わり，鎮痛効果に直接的に影響を与える．

同一の CYP を代謝経路に持つ薬物の併用は，それぞれの薬物の代謝に影響を与える可能性がある．トラマドールと共通の CYP を持つ薬物（**表2**）の相互作用は，すべての組み合わせについて調査されていないが，少なくともブプレノルフィン[15]とオキシコドン[16]は薬物代謝に影響を与えないことが示されており，臨床的に重大な影響を与えるとは考えにくい．

薬物の中には，CYP を阻害することによっ

表3　チトクローム P450 のサブタイプ 2B6，2D6，3A4 を阻害する薬物
（文献 14 から引用改変）

阻害する薬物		CYP サブタイプ		
		2B6	2D6	3A4
オピオイド鎮痛薬	メサドン		低	
抗うつ薬	クロミプラミン		高	
	パロキセチン		高	
	フルボキサミン		低	低
	セルトラリン		低	
NSAIDs 他	セレコキシブ		低	
抗精神病薬	ハロペリドール		高	
	リスペリドン		高	
循環系薬	ニフェジピン			低
	ベラパミル			高
	キニジン		高	
	アミオダロン		高	高
感染症薬	エリスロマイシン			高
	フルコナゾール			高
	クラリスロマイシン			高
	ケトコナゾール			高
	ミコナゾール			高
	リトナビル		低	高
	クロロキン		高	
その他	シメチジン		高	高
	タクロリムス			高
	ジルチアゼム			高
	ジフェンヒドラミン		低	
	グレープフルーツ			低

てトラマドールの代謝を低下させ，血中濃度を上昇させる作用を持つものがある（**表3**）[14]．ただし，M1 のようにトラマドール自体よりもμオピオイド受容体により高い親和性を持ち，鎮痛作用を持つ代謝産物もあるので，CYP 阻害が必ずしも鎮痛効果の増強を示すわけではない．ただし，一般に CYP 阻害は鎮痛効果の増強や副作用の強化につながるといえ，CYP 阻害薬を併用している患者にオピオイド鎮痛薬を導入する際には，転倒・転落の危険性が高まるとする報告もあるので十分な注意が必要である[17]．

酵素阻害をする薬物とは逆に，CYP を誘導することによってトラマドール代謝を促進させ，トラマドールの血中濃度が鎮痛有効量まで上昇することを妨げる薬物もある（**表4**）．こ

表4　チトクローム P450 のサブタイプ 2B6，2D6，3A4 を誘導する薬物
（文献 14 より引用改変）

		CYP		
		2B6	2D6	3A4
抗痙攣薬	カルバマゼピン			高
	フェノバルビタール			高
	フェニトイン			高
	トピラマート			高
その他	リファンピシン			高
	シクロホスファミド			低
	デキサメタゾン			高
	エタノール			低
	ニンニク			低
	セント・ジョーンズ・ワート			低

れらを服用している患者にトラマドールを併用する際には，鎮痛効果が減弱している可能性があるため，トラマドールが無効であるのか鎮痛有効量に達していないのかを副作用の発現にも着目して注意深く評価しなければならない．

薬物以外にも，グレープフルーツは CYP 酵素阻害作用を持ち，エタノール，ニンニクやセント・ジョーンズ・ワートは CYP 酵素誘導作用を持つことが知られている．また，カフェインもトラマドールの鎮痛効果を強化する[18]．したがって，食品や栄養サプリメントにも注意が必要であり，適切な薬物指導や飲酒に関する生活習慣の指導を実施しなければならない．

おわりに

トラマドールは，μオピオイド受容体完全作動作用とセロトニン・ノルアドレナリン再取り込み阻害作用が相乗的に働いて鎮痛効果を発揮し，侵害受容性疼痛と神経障害性疼痛のいずれにも有効なだけでなく，オピオイド鎮痛薬に対する精神依存が非常に少ないことも知られている．強オピオイド鎮痛薬を使用してもコントロール不良な重度の疼痛に，トラマドールを併用することによって十分な鎮痛が得られる報告も多く，単純に弱オピオイド鎮痛薬なので中等度の痛みにしか有効性がないとは決めつけられず，トラマドールを使用する機会は比較的高いと考えられるので，その薬物相互作用を理解することは極めて重要である．

文　献

1) Grond S, Sablotzki A：Clinical pharmacology of tramadol. Clin Pharmacokinet 43：879-923, 2004
2) Collart L, Luthy C, Dayer P：Partial inhibition of tramadol antinociceptive effect by naloxone in man. Br J Clin Pharmacol 35：73, 1993
3) Rao SG, Gendreau JF, Kranzier JK：Understanding the fibromyalgia syndrome. Psychopharmacol Bull 40：24-56, 2008
4) Leong ML, Gu M, Speltz-Paiz R, et al：Neuronal loss in the rostral ventromedial medulla in a rat model of neuropathic pain. J Neurosci 31：17028-17039, 2011
5) Rahman W, Bauer CS, Bannister K, et al：Descending serotonergic facilitation and the antinociceptive effects of pregabalin in a rat

model of osteoarthritic pain. Mol Pain 5 : 45, 2009
6) Romero A, Miranda HF, Puig MM: Antinociceptive effects of morphine, fentanyl, tramadol and their combination in morphine-tolerant mice. Pharmacol Biochem Behav 97 : 363-369, 2010
7) Nishiyori M, Nagai J, Nakazawa T, et al: Absence of morphine analgesia and its underlying descending serotonergic activation in an experimental mouse model of fibromyalgia. Neurosci Lett 472 : 184-187, 2010
8) Lorenzo LD, Foti C, Forte AM, et al: The addition of tramadol as a second opioid may improve pain relief in severe osteoarthritis: Aprospective study. Pain Prac 10 : 540-547, 2010
9) De Witte JL, Schoenmaekers B, Sessler DI, et al: The analgesic efficacy of tramadol is impaired by concurrent administration of ondansetron. Anesth Analg 92 : 1319-1321, 2001
10) Cicero TJ, Inciardi JA, Adams EH, et al: Rates of abuse of tramadol remain unchanged with the introduction of new branded and generic products: Results of an abuse monitoring system, 1994-2004. Pharmacoepidemiol Drug Safe 14 : 851-859, 2005
11) Millan MJ: Descending control of pain. Prog Neurobiol 66 : 355-474, 2002
12) Rauers NI, Stuber F, Lee EH, et al: Antagonistic effects of ondansetron and tramadol?: A randomized placebo and active drug controlled study. J Pain 11 : 1274-1281, 2010
13) Samer CF, Piguet V, Dayer P, et al: Polymorphism and drug interactions: Their importance in the treatment of pain. Can J Anesth 52 : 806-821, 2005
14) Leppert W: CYP2D6 in the embolism of opioids for mild to moderate pain. Pharmacol 87 : 274-285, 2011
15) Coller JK, Michalakas JR, James HM, et al: Inhibition of CYP2D6-mediated tramadol O-demethylation in methadone but not bupurenorphine maintenance patients. Br J Clin Pharmacol 74 : 835-841, 2012
16) Curry SC, Watts DJ, Katz KD, et al: The effect of single-dose tramadol on oxycodone clearance. J Emerg Med 33 : 407-411, 2007
17) Moller J, Laflamme L, Lofdal KS: CYP2D6-inhibiting drugs and the increased risk of fall-related injuries due to newly initiated opioid treatment: A Swedish, register-based case-cross over study. Basic Clin Pharmacol Toxicol 2014 (in press)
18) Diaz-Reval MI, Carrillo-Munguia N, Marrtinez-Casas M, et al: Tramadol and caffeine produce synergistic interactions on antinociception measured in a formalin model. Pharmacol Biochem Behav 97 : 357-362, 2010

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REHABILITATION SECTION

Validation of the Japanese Version of the Pain Self-Efficacy Questionnaire in Japanese Patients with Chronic Pain

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Abstract

Objectives. The present study aimed to develop the Japanese version of the Pain Self-Efficacy Questionnaire (PSEQ-J) and to evaluate its psychometric properties.

Design. Cross-sectional design.

Setting. A pain clinic, a neurosurgery unit, and an orthopedic surgery unit in one university hospital and a pain clinic in a municipal hospital.

Methods. One hundred and seventy-six participants completed study measures, which included 1) the PSEQ-J, 2) the Hospital Anxiety and Depression Scale, 3) the Pain Catastrophizing Scale, 4) the Medical Outcome Study Short-Form 36, 5) the Pain Disability Assessment Scale, and 6) the Short-Form McGill Pain Questionnaire.

Results. The PSEQ-J demonstrated adequate reliability and validity. Hierarchical multiple regression analyses showed that pain self-efficacy as measured with the PSEQ-J accounted for a significant proportion of the variance on the measures administered in the present study. The PSEQ-J was most strongly associated with social activity.

Conclusions. The results demonstrated that the PSEQ-J has adequate psychometric properties, supporting its use in clinical and research settings and suggest that the PSEQ-J may be particularly strongly associated with more social and less physical activity.

Key Words. Self-Efficacy; Chronic Pain; Social Activity

Introduction

Research supports a consistent association between a number of negative cognitive factors, such as fear-avoidance belief [1,2] and catastrophizing [3–5], and chronic pain. The Fear-Avoidance Model [6,7] hypothesizes a critical role for, in particular, these negative cognitive factors in the maintenance and aggravation of chronic pain.

In other models of chronic pain, positive cognitive factors, such as self-efficacy, are hypothesized as protective factors that contribute to adjustment despite pain [8–10]. Self-efficacy is defined by Bandura [11] as "people's judgments of their capabilities to organize and execute courses of action required to attain designated types of performances" (p. 391). In support of this model, self-efficacy beliefs related to pain management have been shown to be associated with a number of key outcome domains in individuals with chronic pain, including: less pain intensity and severity [12–18], more perceived quality of life (QOL) [19–21], more adaptive pain coping [22–25], being more likely to be employed [26], and better pain

treatment outcome [27–29]. Self-efficacy is also consistently associated with less disability [21,25,30–34]. In fact, both Ayre and Tyson [35] and Denison et al. [36] showed that self-efficacy beliefs were stronger predictors of less disability than fear-avoidance beliefs. Furthermore, self-efficacy has been shown to moderate the association between pain intensity and disability [37–40]. As a group, this research suggests that clinicians and researchers should take self-efficacy into consideration when developing models and treatments of chronic pain.

As a type of belief, pain self-efficacy must be assessed via self-report. Common measures of this construct include the Arthritis Self-Efficacy Scale [28], the Chronic Pain Self-Efficacy Scale [41], the Pain Self-Efficacy Questionnaire (PSEQ) [42], and the Self-Efficacy Scale [43]. Among these measures, the PSEQ appears to have the most strengths, in that it is both brief (with only 10 items), yet measures multiple domains of self-efficacy, including self-efficacy regarding social interactions and valued activities, in addition to self-efficacy regarding physical functioning. In a systematic review of pain self-efficacy measures, Miles et al. [44] concluded that the PSEQ was among the most reliable. The PSEQ has also been used in a variety of clinical settings [29,35,45–50], supporting its potential utility.

The PSEQ has been translated into Chinese [51,52], Dutch [53], Persian [54], and Portuguese [55], with each version evidencing good psychometric properties. Although there are versions of the PSEQ in several languages, a psychometrically sound Japanese version has not yet been developed. Furthermore, there are no other psychological measures specific to pain self-efficacy in Japanese. Such a measure is needed to determine the extent to which the importance of the self-efficacy construct to adjustment to chronic pain is universal; that is, to replicate the findings regarding self-efficacy in Western pain populations in Japanese samples. Hence, the present study aims to develop and evaluate the psychometric properties of the Japanese version of the PSEQ (PSEQ-J). If valid, we hypothesized the PSEQ-J would be positively associated with measures of positive adaptation (e.g., social functioning) and negatively associated with measures of dysfunction (e.g., pain interference, depression) in a sample of Japanese patients with chronic pain. We also hypothesized nonsignificant correlation between the PSEQ-J and the pain severity because previous studies did not show their significant correlation [42,51,52,54]. By examining these associations, the current study will also allow us to extend previous findings to determine the association between pain self-efficacy and important outcome domains that have not yet been adequately studied.

Methods

Participants

Participants were outpatients with chronic pain who were examined in the pain clinic, neurosurgery unit, and orthopedic surgery unit in a university hospital, and the pain clinic in a municipal hospital. Study inclusion criteria were 1) history of pain for 6 months or more, 2) age 16 years or older, 3) ability to read and write Japanese, and 4) willingness to participate in the present study.

Measures

PSEQ-J

The PSEQ is a 10-item self-report questionnaire designed to assess the degree of confidence in performing a number of activities despite pain. Each item is rated on a 7-point Likert-type scale (0 = not at all confident, 6 = completely confident). Total scores can range from 0 to 60, and a higher score indicates greater self-efficacy for functioning despite pain.

All of other language versions of the PSEQ have been found to have high internal consistencies (original version Cronbach's $\alpha = 0.92$, Brazilian version Cronbach's $\alpha = 0.90$, Chinese version Cronbach's $\alpha = 0.93$ and 0.94, Dutch version Cronbach's $\alpha = 0.90$ and 0.92, Persian version Cronbach's $\alpha = 0.92$) [42,51–55]. Previous studies have also found that the PSEQ has a one-factor structure, using both exploratory factor analysis [42,51,53,55] and confirmatory factor analysis [52–54].

Our translation process was conducted according to the following four steps. First, the first author (TA) translated all of the original PSEQ items from English into Japanese. This initial translation was then checked by the last author (JS, who is fluent in Japanese and English). Any differences in the meaning and clarity of the translated items between the first and last authors were discussed and resolved via consensus. In a third step, the revised Japanese version (PSEQ-J) was back-translated from Japanese into English by a native English speaker who was also fluent in Japanese. Finally, the back-translation was checked and approved by the developer of the original PSEQ.

Validity Criterion Measures

Five pain-related outcomes were assessed as validity criterion assessing: negative affectivity, pain catastrophizing, health-related QOL, pain interference, and pain severity. These domains were selected both because 1) they reflect many of the outcomes that have been shown to be associated with pain self-efficacy in previous research and 2) they assess domains recommended as core pain-related factors that should be assessed in pain clinical trials [56,57].

Negative Affectivity: Hospital Anxiety and Depression Scale (HADS). The HADS is a 14-item self-report questionnaire of negative affectivity developed for population of patients with physical illness [58,59]. Each item is rated on a 4-point Likert-type scale. The HADS is scored to create two subscales (measuring anxiety and depression). The Japanese version of the HADS used in this study has

evidence supporting its reliability, with Cronbach's α coefficients of >0.80 for the Anxiety subscale and >0.70 for the Depression subscale [60].

Pain Catastrophizing: Pain Catastrophizing Scale (PCS). The PCS is a 13-item self-report questionnaire that measures maladaptive thoughts regarding pain [61]. Each item is rated on a 5-point Likert-type scale. The PCS can be scored to create three subscales assessing helplessness, magnification and rumination, and total score. The Japanese version of the PCS used in this study has been shown to have excellent reliability except for magnification subscale. These Cronbach's α coefficients are 0.81 for the Helplessness subscale, 0.65 for the Magnification subscale, 0.80 for the rumination subscale, and 0.89 for the total score [62].

Health-Related QOL: Medical Outcome Study Short-Form 36 (SF-36). The Medical Outcome Study SF-36 is a 36-item scale measuring health-related QOL [63]. The SF-36 assesses eight quality-of-life domains related to physical and mental health (Physical Functioning, Role Physical, Bodily Pain, Social Functioning, General Health, Vitality, Role Emotional, and Mental Health). Scores in each category can range from 0 to 100, and higher scores indicate better QOL. Fukuhara et al. developed the Japanese version of the SF-36 and found that Cronbach's α coefficients for all eight scales were >0.70 [64].

Pain Interference: Pain Disability Assessment Scale (PDAS). The PDAS is a 20-item self-report questionnaire measuring pain-related interference in three domains of functioning: the Activities using the Low Back subscale, the Activities of Daily Living subscale, and the Social Activities subscale [65]. Each item is rated on a 4-point Likert-type scale. The total score of the PDAS and three subscales evidenced excellent reliability, with Cronbach's α coefficients ranging from 0.87 to 0.95.

Pain Severity: Short-Form McGill Pain Questionnaire (MPQ-SF). The MPQ-SF (MPQ-SF © Ronald Melzack, 1984. All Rights Reserved. MPQ-SF contact information and permission to use: MAPI Research Trust, Lyon, France. E-mail: PROinformation@mapi-trust.org; Internet: http://www.mapi-trust.org) is a 15-item questionnaire assessing sensory and affective dimensions of pain experience [66]. Each item is rated on a 4-point Likert-type scale. The MPQ-SF can be scored to create two subscales assessing the sensory and affective dimensions of pain. Arimura et al. developed the Japanese version of the MPQ-SF and reported it had sufficient reliability, with Cronbach's α coefficients of 0.80 for the Sensory subscale, 0.78 for the Affective subscale, and 0.87 for the total score [67].

Procedures

Participants were asked to complete all the scales at once while waiting for their consultation. A subset of these participants who returned for a second consultation (range, 6–91 days after the first consultation, median = 28 days) were asked to complete all of the study measures again. The study was approved by the Institutional Review Board for Clinical Research at Osaka University Hospital, and written informed consent were obtained by all participants before they completed the measures. None of the participants were enrolled in an intervention program targeting pain self-efficacy at any of the four locations. Data were collected from May 2012 to September 2012.

Statistical Analysis

Statistical analyses were conducted using Statistical Package for the Social Sciences 17.0 (IBM Japan, Tokyo, Japan). Demographic characteristics of participants were analyzed using descriptive statistics. Cronbach's α coefficient was calculated to evaluate the internal consistency of the PSEQ-J. Intraclass correlations (ICCs) were also calculated to assess test–retest reliability. The factor structure of the PSEQ-J was analyzed using exploratory factor analysis. We expected to get the one-factor solution of the PSEQ-J because previous studies have shown the appropriateness of the one factor solution for the PSEQ [42,51–55].

We computed the Pearson correlation coefficients between the PSEQ-J and the validity criterion measures to evaluate the concurrent validity of the PSEQ-J. Because of the large number of coefficients computed, we set strict criteria in order to determine that an association was statistically significant. Specifically, we determine that only correlations with absolute values of 0.40 or greater and with *P* values of 0.001 or less were considered significant. These same criteria were adopted in previous studies developing the original and other language version of the PSEQ [42,51,52,54]. Finally, we used three-step hierarchical multiple regression analyses to assess the predictive power of the PSEQ-J on other dependent variables when controlling demographic variables and pain severity. The variables demonstrating significant correlations with the PSEQ-J in the univariate analyses were chosen as dependent variables in the regression analyses.

Results

Study Enrollment Flow and Demographic Characteristics of Participants

Two hundred and thirty-four patients agreed to participate in the study and completed at least some of the measures at the initial assessment. However, 50 of these participants did not complete all of the measures, and eight participants were subsequently found to have had pain for less than 6 months, and so were excluded from the analyses. This left 176 participants (80 males and 96 females) with complete data. The mean age of the final sample was 64.33 years (standard deviation [SD] = 15.12). A total of 87 participants (51 males and 36 females) completed the questionnaires twice. The mean age of these individuals was 67.00 years (SD = 12.39). The mean duration between the first and second survey was 34.84 days (SD = 19.11).

Duration of pain among 176 participants were as follows: from 6 months to 1 year (N = 13; 7%), from 1 year to 3 years (N = 25; 14%), from 3 years to 5 years (N = 30; 17%), and over 5 years (N = 108; 61%). Thus, the majority of participants in our study had experienced intractable pain for over 5 years. Pain types were as follows: low back pain (N = 46; 26%), leg pain (N = 90; 51%), herpes zoster and postherpetic neuralgia (N = 10; 6%), complex regional pain syndrome (N = 2; 1%), poststroke pain (N = 14; 8%), traumatic brachial plexus injury (N = 5; 3%), migraine (N = 15; 9%), other types of chronic headache (N = 9; 5%), neck pain (N = 7; 4%), cancer pain (N = 1; 1%), and other pain (N = 23; 13%). A total of 39 participants (22%) reported more than two types of pain. Most of the participants (N = 157; 89%) had at least a high school education. Most of the participants (N = 117; 66%) were not employed. The reminder worked full time (N = 38; 22%), part time (N = 17; 10%), or were students (N = 4; 2%). The majority of the participant reported that they had ever received the following treatments for pain: pharmacotherapy (N = 159; 90%), procedural intervention like a surgery and a nerve block (N = 89; 51%), and other treatments (N = 4; 2%). A total of 79 participants (45%) reported that they had ever received two or more types of pain treatment. The mean PSEQ-J score was 33.06 (SD = 13.51). The scores for other study measures are reported in Table 1.

Table 1 Mean, SD, and range of scores of psychological measures (N = 176)

Measures	Mean	SD	Range
PSEQ-J (0–60)	33.06	13.51	0–60
MPQ-SF-Sensory (0–33)	7.89	6.45	0–30
MPQ-SF-Affective (0–12)	2.10	2.83	0–12
MPQ-SF-Total (0–45)	9.99	8.66	0–40
SF-36-Physical Functioning (0–100)	59.74	25.96	0–100
SF-36-Role Physical (0–100)	57.78	30.42	0–100
SF-36-Bodily Pain (0–100)	40.82	19.96	0–100
SF-36-General Health (0–100)	48.56	19.64	0–100
SF-36-Vitality (0–100)	50.39	21.12	0–100
SF-36-Social Functioning (0–100)	65.84	27.78	0–100
SF-36-Role Emotional (0–100)	65.77	31.41	0–100
SF-36-Mental Health (0–100)	60.20	22.34	0–100
HADS-Anxiety (0–21)	5.48	3.77	0–19
HADS-Depression (0–21)	5.90	4.08	0–21
HADS-Total (0–42)	11.38	7.07	0–40
PCS-Rumination (0–20)	13.41	4.95	0–20
PCS-Helplessness (0–20)	8.46	5.55	0–20
PCS-Magnification (0–12)	4.60	3.30	0–12
PCS-Total (0–52)	26.47	12.16	0–52
PDAS-Activities Using the Low Back (0–15)	6.48	4.24	0–15
PDAS-Activities of Daily Living (0–21)	4.56	4.48	0–18
PDAS-Social Activities (0–24)	8.83	6.83	0–24
PDAS-Total (0–60)	19.87	14.19	0–52

Note: HADS = Hospital Anxiety and Depression Scale; PCS = Pain Catastrophizing Scale; PDAS = Pain Disability Assessment Scale; PSEQ-J = the Japanese version of the Pain Self-Efficacy Questionnaire; MPQ-SF = Short-Form McGill Pain Questionnaire; SF-36 = Medical Outcomes Study 36-Item Short-Form Health Survey.

Reliability of the PSEQ-J

The PSEQ-J evidenced excellent reliability, with an internal consistency (Cronbach's α) coefficient of 0.94. Moreover, the values for Cronbach's α coefficient if one item was deleted ranged from 0.93 to 0.95. Moderate to high item–total correlations were found, ranging from 0.50 to 0.86. These findings indicate that all items were strongly associated with the total score. Factor loadings for all items exceeded 0.50.

The overall test–retest stability ICC of the PSEQ-J was 0.80 (95% confidence interval: 0.71–0.87). ICCs of individual items ranged from 0.59 to 0.69. The ICC between two measurement points indicated that the PSEQ-J had substantial stability over time, on the basis of the criteria proposed by Landis and Koch [68].

The statistics related to reliability of the PSEQ-J are summarized in Table 2.

Validity

The exploratory factor analysis yielded a one-factor solution was obtained based on the Kaiser Criterion, which accounted for 66% of the total variance (Table 3). The minimal factor loading was 0.51 (item 7). As only one factor was extracted, the solution was not rotated. Although item 7 had the lowest factor loading and the lowest item–total correlation (item–total correlation = 0.50), the loading exceeded the threshold (0.30 or 0.40) recommended by Floyd and Widaman [69]. This same pattern of results was found in previous studies on the PSEQ [42,51,55]. Hence, item 7 was retained in the PSEQ-J.

The Pearson correlation coefficients between the PSEQ-J and the validity criterion are presented in Table 4. Significant negative correlations were found between the PSEQ-J scores and the measures of anxiety, depression, the total scores of negative affectivity, three catastrophizing subscales (assessing rumination, helplessness, and magnification), total catastrophizing score, social activity interference, and total pain interference (rs = –0.43, –0.44, –0.49, –0.46, –0.43, –0.40, –0.49, –0.51, and –0.43, respectively). Significant positive correlations were found between the PSEQ-J score and the score of the Role Physical, the Bodily Pain, the Vitality, the Social Functioning, the Role Emotional, and the Mental Health of the SF-36 (rs = 0.41, 0.45, 0.46, 0.43, 0.41, and 0.40, respectively). The associations between the PSEQ-J and the measures of pain severity were not statistically significant (see Table 4).

Table 2 Intraclass correlations (ICCs), item–total correlations, Cronbach's α if item deleted, item means and SD, and factor loadings for the PSEQ-J

Item	Intraclass Correlation (95% CI)	Item–Total Correlation	Cronbach's α if Item Deleted	Mean	SD	Factor Loading
1. I can enjoy things . . .	0.66 (0.53–0.77)	0.74	0.93	3.35	1.69	0.77
2. I can do most . . .	0.59 (0.43–0.71)	0.75	0.93	3.37	1.74	0.77
3. I can socialise with . . .	0.59 (0.44–0.71)	0.78	0.93	3.82	1.70	0.81
4. I can cope with . . .	0.63 (0.49–0.74)	0.79	0.93	3.48	1.56	0.82
5. I can do some . . .	0.69 (0.56–0.78)	0.81	0.93	3.49	1.67	0.84
6. I can still do . . .	0.69 (0.57–0.79)	0.76	0.93	3.38	1.67	0.79
7. I can cope with . . .	0.65 (0.51–0.76)	0.50	0.95	2.41	1.83	0.51
8. I can still accomplish	0.66 (0.52–0.76)	0.81	0.93	3.12	1.68	0.84
9. I can live a normal . . .	0.69 (0.57–0.79)	0.86	0.93	3.43	1.65	0.89
10 I can gradually become . . .	0.68 (0.55–0.78)	0.78	0.93	3.22	1.56	0.81

Relationships Between Self-Efficacy and QOL, Negative Affectivity, Catastrophizing, and Pain Interference

The results of the hierarchical regression analyses examining the relationships between pain self-efficacy and six of the QOL domains assessed by the SF-36, after controlling for patient characteristics (i.e., age, gender, and pain duration) and pain severity (as measured by the total score of the MPQ-SF), are presented in Table 5. The results of the hierarchical regression analyses examining the relationships between pain self-efficacy and nine of the dysfunction measures assessed by the HADS, the PCS, and the PDAS, after controlling for same variables, are also presented in Table 6.

Patient characteristics accounted for a significant proportion of the variance in the scores assessing rumination catastrophizing, helplessness catastrophizing, catastrophizing total score, social activity interference, and total

Table 3 Eigenvalues for the PSEQ-J

	Initial Eigenvalue		
Component	Total	% of Variance	Cumulative %
1	6.600	65.999	65.999
2	0.845	8.446	74.445
3	0.593	5.934	80.379
4	0.542	5.416	85.796
5	0.355	3.546	89.342
6	0.262	2.615	91.957
7	0.238	2.383	94.340
8	0.227	2.273	96.614
9	0.199	1.992	98.606
10	0.139	1.394	100.000

Table 4 Pearson correlations between the PSEQ-J and other measures

Measures		Correlation Coefficient (r)	*P*
MPQ-SF	Sensory	–0.18	<0.020
	Affective	–0.32	<0.001
	MPQ-SF-Total	–0.24	<0.002
SF-36	Physical Functioning	0.24	<0.002
	Role Physical	0.41*	<0.001
	Bodily Pain	0.45*	<0.001
	General Health	0.31	<0.001
	Vitality	0.46*	<0.001
	Social Functioning	0.43*	<0.001
	Role Emotional	0.41*	<0.001
	Mental Health	0.40*	<0.001
HADS	Anxiety	–0.43*	<0.001
	Depression	–0.44*	<0.001
	HADS-Total	–0.49*	<0.001
PCS	Rumination	–0.46*	<0.001
	Helplessness	–0.43*	<0.001
	Magnification	–0.40*	<0.001
	PCS-Total	–0.49*	<0.001
PDAS	Activities Using the Low Back	–0.30	<0.001
	Activities of Daily Living	–0.30	<0.001
	Social Activities	–0.51*	<0.001
	PDAS-Total	–0.43*	<0.001

Note. Due to the large number of correlations, strict criteria were set for significance: *$r \geq 0.40$, $P \leq 0.001$ ($N = 176$). HADS = Hospital Anxiety and Depression Scale; PCS = Pain Catastrophizing Scale; PDAS = Pain Disability Assessment Scale; MPQ-SF = Short-Form McGill Pain Questionnaire; SF-36 = Medical Outcomes Study 36-Item Short-Form Health Survey.

Table 5 Results of hierarchical multiple regression analysis on predictors of six subscales of the SF-36

Dependent Variables	Predictors	Total R^2	$\triangle R^2$	*F*-change	Beta to Enter	*t*
Role Physical	Step 1: Demographic variables	0.01	0.01	0.67		
	Age				−0.09	−1.23
	Gender				0.02	0.27
	Pain duration				−0.05	−0.68
	Step 2: Pain severity	0.16	0.15	30.44**	−0.39**	−5.52
	Step 3: Pain self-efficacy	0.31	0.14	35.37**	0.42**	5.95
Bodily Pain	Step 1: Demographic variables	0.04	0.04	2.36		
	Age				0.13	1.78
	Gender				−0.03	−0.35
	Pain duration				−0.13	−1.74
	Step 2: Pain severity	0.36	0.32	84.95**	−0.57**	−9.22
	Step 3: Pain self-efficacy	0.45	0.09	26.98**	0.33**	5.19
Vitality	Step 1: Demographic variables	0.04	0.04	2.49		
	Age				0.14	1.83
	Gender				−0.14	−1.82
	Pain duration				0.06	0.75
	Step 2: Pain severity	0.13	0.09	18.24**	−0.31**	−4.27
	Step 3: Self-efficacy	0.29	0.16	38.11**	0.44**	6.17
Social Functioning	Step 1: demographic variables	0.00	0.00	0.19		
	Age				−0.03	−0.43
	Gender				0.03	0.39
	Pain duration				−0.04	−0.53
	Step 2: Pain severity	0.16	0.16	31.63**	−0.40**	−5.62
	Step 3: Pain self-efficacy	0.31	0.15	36.14**	0.42**	6.01
Role Emotional	Step 1: Demographic variables	0.02	0.02	0.98		
	Age				−0.12	−1.62
	Gender				0.02	0.29
	Pain duration				−0.04	−0.47
	Step 2: Pain severity	0.14	0.12	23.62**	−0.35**	−4.86
	Step 3: Pain self-efficacy	0.30	0.16	39.09**	0.44**	6.25
Mental Health	Step 1: Demographic variables	0.04	0.04	2.17		
	Age				0.02	0.31
	Gender				−0.17*	−2.28
	Pain duration				0.10	1.35
	Step 2: Pain severity	0.15	0.11	22.63**	−0.34**	−4.76
	Step 3: Pain self-efficacy	0.30	0.15	35.56**	0.42**	5.96

Note. $^{**}P < 0.01$, $^{*}P < 0.05$.

pain interference (5–7%). However, patient characteristics accounted for a nonsignificant proportion of the variance in the six QOL scales. Pain severity accounted for a significant proportion of the variance in the six QOL scales (9–32%) and other dependent variables (10–20%). More severe pain predicted lower QOL and higher negative affectivity, catastrophizing, and pain interference.

The third step of the analysis revealed that pain self-efficacy was a significant and substantial predictor of QOL, negative affectivity, catastrophizing, and pain interference over and above the control variables. Pain self-efficacy accounted for a significant proportion of the variance in the six QOL scales (9–16%) and other dependent variables (9–27%). Higher pain self-efficacy was associated with higher QOL and lower negative affectivity, pain catastrophizing, and pain interference. Although pain self-efficacy was significantly associated with many of the criterion variables, it demonstrated the strongest (negative) association (27% unique variance accounted for after controlling for demographic variables and pain severity) with social activity interference.

Discussion

The aim of the present study was to evaluate the psychometric properties of the PSEQ-J in a sample of Japanese patients with chronic pain. Our results showed that the PSEQ-J had excellent internal consistency and test–retest reliability and that the PSEQ-J had one-factor structure,

Table 6 Results of hierarchical multiple regression analysis on predictors of negative affectivity, catastrophizing, and pain interference

Dependent Variables	Predictors	Total R^2	$\triangle R^2$	*F*-change	Beta to Enter	*t*
Anxiety	Step 1: Demographic variables	0.03	0.03	1.93		
	Age				−0.14	−1.83
	Gender				0.04	0.55
	Pain duration				0.09	1.20
	Step 2: Pain severity	0.21	0.18	39.73**	0.43**	6.30
	Step 3: Pain self-efficacy	0.31	0.10	24.38**	−0.35**	−4.94
Depression	Step 1: Demographic variables	0.01	0.01	0.61		
	Age				0.04	0.52
	Gender				−0.03	−0.39
	Pain duration				0.09	1.24
	Step 2: Pain severity	0.14	0.13	25.31**	0.36**	5.03
	Step 3: Pain self-efficacy	0.30	0.16	38.41**	−0.44**	−6.20
HADS Total	Step 1: Demographic variables	0.01	0.01	0.81		
	Age				−0.05	−0.67
	Gender				0.01	0.07
	Pain duration				0.10	1.35
	Step 2: Pain severity	0.20	0.19	40.34**	0.44**	6.35
	Step 3: Pain self-efficacy	0.36	0.16	41.93**	−0.44**	−6.47
Rumination	Step 1: Demographic variables	0.05	0.05	3.33**		
	Age				−0.05	−0.70
	Gender				−0.10	−1.37
	Pain duration				0.22**	2.91
	Step 2: Pain severity	0.21	0.15	33.04**	0.40**	5.75
	Step 3: Pain self-efficacy	0.33	0.12	31.48**	−0.39**	−5.61
Helplessness	Step 1: Demographic variables	0.05	0.05	3.05*		
	Age				−0.10	−1.40
	Gender				−0.01	−0.20
	Pain duration				0.20**	2.60
	Step 2: Pain severity	0.25	0.20	46.08**	0.45**	6.79
	Step 3: Pain self-efficacy	0.34	0.09	23.03**	−0.33**	−4.80
Magnification	Step 1: Demographic variables	0.02	0.02	1.23		
	Age				0.05	0.63
	Gender				0.03	0.37
	Pain duration				0.13	1.74
	Step 2: Pain severity	0.12	0.10	19.97**	0.32**	4.47
	Step 3: Pain self-efficacy	0.25	0.13	28.49**	−0.39**	−5.34
PCS Total	Step 1: Demographic variables	0.05	0.05	2.96*		
	Age				−0.06	−0.75
	Gender				−0.04	−0.54
	Pain duration				0.21**	2.85
	Step 2: Pain severity	0.25	0.20	46.60**	0.46**	6.83
	Step 3: Pain self-efficacy	0.39	0.14	39.66**	−0.41**	−6.30
Social Activities	Step 1: Demographic variables	0.05	0.05	2.74*		
	Age				0.14	1.86
	Gender				0.12	1.62
	Pain duration				0.11	1.47
	Step 2: Pain severity	0.15	0.10	20.01**	0.32**	4.47
	Step 3: Pain self-efficacy	0.41	0.27	76.54**	−0.57**	−8.75
PDAS Total	Step 1: Demographic variables	0.07	0.07	4.05**		
	Age				0.19*	2.60
	Gender				0.12	1.66
	Pain duration				0.13	1.71
	Step 2: Pain severity	0.19	0.13	26.94**	0.36**	5.19
	Step 3: Pain self-efficacy	0.38	0.19	52.37**	−0.48**	−7.24

Note. $^{**}P < 0.01$, $^{*}P < 0.05$. HADS = Hospital Anxiety and Depression Scale; PCS = Pain Catastrophizing Scale; PDAS = Pain Disability Assessment Scale.

consistent with studies validating the PSEQ in other languages [42,51–55]. Moreover, consistent with our hypotheses, we found significant positive associations between the PSEQ-J and the six QOL scales of the SF-36, and significant negative associations between the PSEQ-J and negative affectivity, pain catastrophizing, and pain interference. We also found the nonsignificant association between the PSEQ-J and pain severity. These findings support the concurrent validity of the PSEQ-J. The PSEQ-J was also shown to be a significant predictor of QOL, negative affectivity, pain catastrophizing, and pain interference in our sample of Japanese patient with chronic pain. Overall, the findings support the psychometric soundness of the PSEQ-J.

The correlation between PSEQ-J and pain severity measured with the MPQ-SF was not statistically significant, as hypothesized. This finding is consistent with the results reported by previous studies developing and validating the PSEQ [42,51,52,54]. Consistent with these findings, a number of clinical studies have found improvements in pain self-efficacy to be associated with decreases in disability, but not pain severity [70,71]. These results support the discriminant validity of the PSEQ-J in general and the PSEQ-J in particular. Although there was a significant association between the SF-36 Bodily Pain scale and the PSEQ-J, the Bodily Pain scale is a composite score made up of ratings of pain and pain interference. Thus, an association between the SF-36 Bodily Pain scale and the PSEQ-J could be anticipated, given that consistent associations between PSEQ scales and measures of disability and pain interference.

There were no significant correlations between the PSEQ-J and pain interference with either the Activities Using the Low Back subscale or the Activities of Daily Living subscale of the PDAS, and with the Physical Functioning scale of the SF-36. On the other hand, the PSEQ-J was significantly correlated with the Social Activities subscale of the PDAS (measuring pain interference with social activities), and the Social Functioning scale of the SF-36. These results suggest that the PSEQ may reflect pain interference with social activity more than interference with physical activity in Japanese chronic pain populations. Although there was a significant positive correlation between the PSEQ-J and the Role Physical scale of the SF-36, which represents a physical role function, four items in the Role Physical scale also refer to the role function related to social activities (e.g., work) [64]. Other researchers have also found that the PSEQ is associated more strongly with measures of social functioning than with measures of physical functioning [51–54]. This tendency thus appears to be a psychometric characteristic of the PSEQ across cultures. However, Lledo-Boyer et al. [72] reported that pain self-efficacy was more closely associated with the physical dysfunction than the psychosocial dysfunction including the Social Interaction category of the Sickness Impact Profile [73] among Spanish fibromyalgia patients. This suggests the possibility of at least some cultural differences in how self-efficacy is related to patient functioning. Further research is needed to explore this possibility.

The present study found a nonsignificant correlation between the PSEQ-J and the General Health scale of the SF-36. Previous studies conducted in East Asian areas also did not confirm a significant correlation between these variables [51,52]. However, Asghari and Nicholas [54] conducted the study in a different cultural area from Japan and reported a significant correlation between measures of these domains. Thus, the strength of the association between pain self-efficacy and feelings of general health may depend, at least in part, on cultural differences. To confirm this proposition, further research is needed to explore the cultural influence on pain-related self-efficacy and subjective health status.

The findings that the PSEQ-J is a significant predictor of negative affectivity, pain catastrophizing, QOL, and especially interference with social activities suggest that psychological interventions to increase pain self-efficacy may improve adjustment of Japanese chronic pain patients. Studies conducted in samples of individuals with chronic pain in other countries reported that cognitive behavioral treatments (CBTs) improving pain self-efficacy simultaneously lead to improvement in other pain-related variables [70,71,74–76]. Most of the participants in the current study reported only pharmacological and procedural interventions as their chronic pain treatments, and psychological interventions are not yet popular in Japanese pain management settings [77]. An important next step is to examine the potential efficacy of psychological interventions that target improvements in pain self-efficacy in samples of Japanese patients with chronic pain. The PSEQ-J may be particularly useful in this research to help determine whether improvements associated with these treatments are effective due to the changes they produce in self-efficacy.

The Japanese mean score of the PSEQ (33.1; SD = 13.5) was greater than that of Australian (25.8; SD = 12.4 [42]), Dutch tertiary care (29.1; SD = 11.0 [53]), and UK (24.1; SD = 11.4 [76]) samples. However, it was lower than the mean PSEQ score of Brazilian (34.8, SD = 14.8 [55]), Dutch primary care (36.3; SD = 12.4 [53]), and Persian (36.0, SD = 14.2 [54]) samples. The mean score of the PSEQ-J in this study was also greater than both the mean PSEQ score in normative data collected at the Australian pain clinic (25.5; SD = 13.8) and the mean PSEQ score of corresponding age group (28.5; SD = 14.4; the 61–70 years old group) [78]. These scores showed that the Japanese sample had moderate pain self-efficacy compared with samples from other cultures and with normative data. Two different mean scores were reported from the Chinese PSEQ. Although Lim et al. reported lower mean scores than our Japanese data (28.5; SD = 13.3) [51], Vong et al. reported the highest mean score in studies validating the PSEQ (40.1; SD = 11.0) [52]. Japanese culture is part of East Asian culture, and the same is true for Chinese culture. Vong et al. speculated that the highest PSEQ score came from the higher tolerance of Chinese