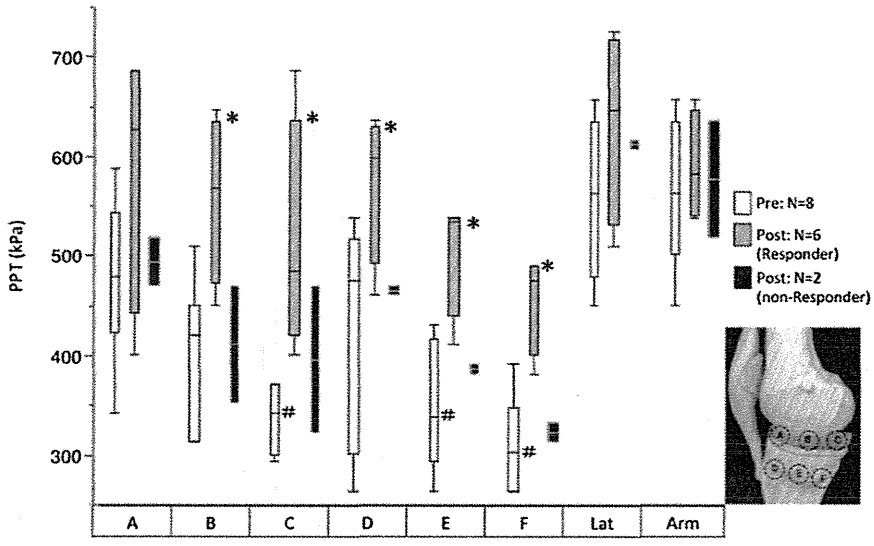

Figure 5 PPTs at pre- and post-treatment. White bar indicates pre- treatment PPTs (n = 8). Gray and black bar indicate post-treatment PPTs of responder (n = 6) and non-responder (n = 2), respectively. # : $p < 0.05$ compared with Arm at pre-treatment. *: $p < 0.05$ compared with pre-treatment in responders. Sonications were applied to the site D, E, F.

undergone TKA for her right knee 5 months ago, and been scheduled surgery for her left knee. She had medial knee pain with the VAS of 78 mm and tenderness on her medial joint space and tibia plateau (pre-treatment median PPT values in the medial knee: 280 kPa). After treatment, she reported dramatic and long-lasting reduction in her left knee pain with PPTs increase (post-treatment median PPT values: 456 kPa). The clinical score was improved from 50 points in pre- to 75 points in post-treatment. At the 18-month follow-up, she was no longer suffering from severe knee pain in her daily life, and canceled her surgery. Figure 7 showed the radiological changes in this patient. MRI showed a low intensity curved line at the sonication site in T1 and T2 weighted images. In X-ray films, an osteosclerotic change was seen in accordance with the low intensity curved line in MRI. There were no findings of OA progression, osteonecrotic change, or segmental collapse of tibia plateau during follow-up period. The other patients also showed similar courses of radiographic change after treatment.

Discussion

This is the first report of clinical application of MRgFUS for knee OA. Real-time monitoring of the sonication area and temperature elevation enabled performance of safe and accurate treatment. Even though the inclusion was restricted to most severe OA in this pilot study, 75% of patients showed successful pain relief. Similar to previous reports of bone metastases [13-15] or lumbar facet

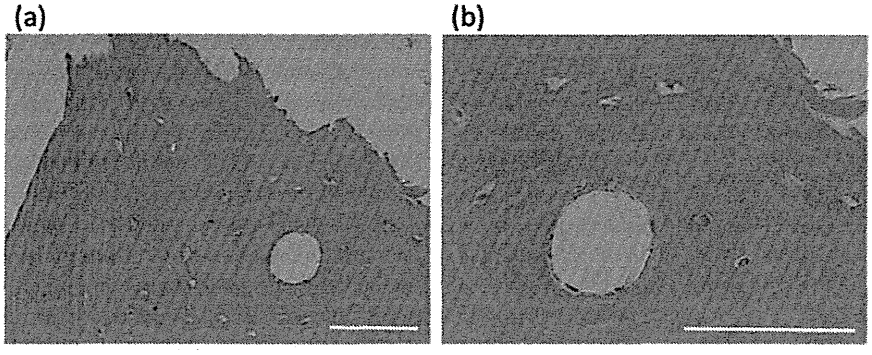

Figure 6 Histology of the bone sample in the treated area. (a) low magnification, **(b)** high magnification. No significant focal bone necrosis was observed. Scale bar: 50 μm.

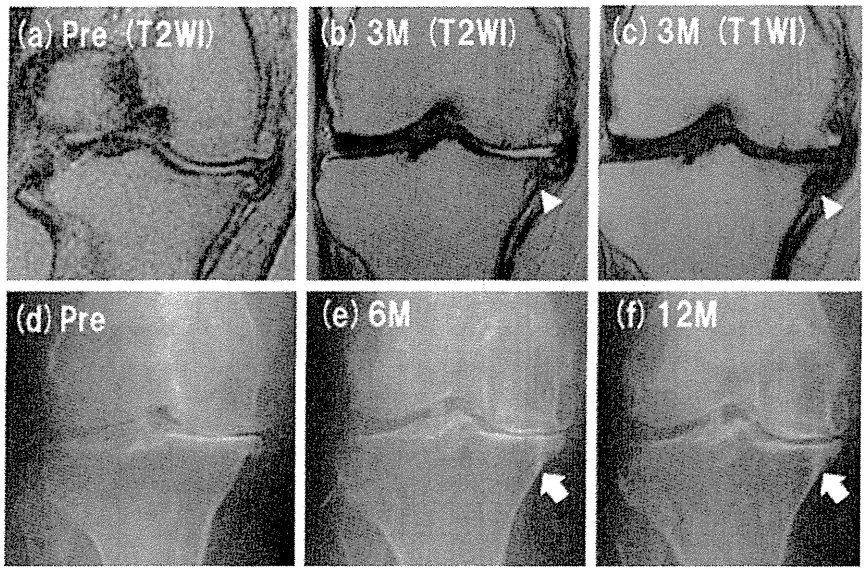

Figure 7 Radiological changes between treatments. (a) MRI (pre-, T2WI), **(b)** MRI (3 months post-, T2WI), **(c)** MRI (3 months post-, T1WI), **(d)** X-p (pre-), **(e)** X-p (6 months post-), **(f)** X-p (12 months post-). Arrow heads in MRI indicate low intensity curved line at the sonication site. Arrows in X-p indicate osteosclerotic change in accordance with the line in MRI.

OA [16], the pain alleviation was rapid and long-lasting. Unlike a conventional transducer integrated with MRI table, a newly developed conformal sonication device was a good fit for extremities and enabled easier treatment of knee OA. Intravenous sedation and opioid administration were not necessary for our treatment, which were applied in the previous series of bone metastases [13-15] or low back pain [16]. Local anesthesia with ropivacaine around the periosteum was enough to reduce pain associated with sonication. Patients were able to relax throughout the procedure and to walk soon after treatment.

The mechanism of pain alleviation is most likely local denervation caused by the heat denaturation of the treated area. However, no previous studies have suggested an assessment method to estimate the denervated area of MRgFUS. In this regard, pressure algometry is a quite simple and useful tool for quantitative evaluation after denervation treatment. Reliable repeated PPT measurements around knee joint have been documented by means of locating the assessment sites in relation to bone landmark [20]. In the present study, all sites in medial knee were easily identified based on the location of joint space, medial collateral ligament and tibial osteophyte, enabling to retest PPTs in a reproducible manner. In our patients who responded to the treatment with pain reduction, PPTs on sonication area were significantly increased after treatment, which means that patients felt less pain by pressure stimulation after denervation. The patients who did not respond to the treatment did not show increased pressure pain thresholds which may suggest that an PPT increase would be a necessary condition of successful treatment. Future studies will be needed to verify if earlier follow-up assessments may be used to predict treatment success.

In this series, all sonications were applied to bone surface just below the rim osteophyte of medial tibia plateau. From a pathophysiological perspective it has been reported that sensory nerve invasion containing substance P and calcitonin gene related peptide was seen in tibial osteophyte in human OA patients [21]. Because surface area of the tibial rim osteophyte itself was a bit narrow to plan sonication, the base of the osteophyte was treated instead. Furthermore, lower PPTs were observed in this area at pre-treatment in all patients and this is also a general finding in OA knees [17]. In other words, hypersensitivity of nociceptive nerve terminals against pressure stimulation was seen in this area, which was preferable for denervation treatment. From a practical perspective there were other reasons to select the treated area. Firstly, bone is a better indication for MRgFUS than soft tissues. Lower thermal conductivity and higher ultrasound absorption rate of cortical bone allows the denervation treatment safe and efficient, which had been demonstrated in previous reports [13-16]. Secondly, tibial rim osteophyte was a good landmark for reproducible planning, treatment and assessment.

The osteosclerotic change after the treatment was interesting. In our patients, the temperature elevation of bone surface was aimed at 60°C because protein

denaturation occurred above the temperature of 57–60°C for a few seconds [22,23]. The goal temperature was almost same as previous publications, and some authors found similar new bone formation after the treatment of bone metastases [13,14]. The mechanism of osteosclerotic change in the treated area is unknown. Although it cannot be excluded that minor thermal or non-thermal bone damage occurred, new bone formation might be an encouraging radiological finding of this therapy [24]. Including its relation to the long-lasting pain relief, further basic research of treated bone marrow would be necessary to assess this phenomenon.

According to the pain alleviation mechanism and results of this study, a good candidate for MRgFUS treatment is patient presenting with localized medial pain, lower PPTs around tibial osteophyte, and no bone marrow lesion or osteonecrosis. In this series, two patients did not respond the treatment. One patient complained spreading medial knee pain and the other had small bone marrow lesion in medial femoral condyle and tibia plateau. Detailed assessment of pain distribution, pressure pain sensitivity, and MRI examination before the treatment might be essential to achieve satisfactory results.

Percutaneous radiofrequency treatment has been reported as a beneficial local denervation therapy for knee OA [4,25]. Comparing with radiofrequency, MRgFUS treatment has some advantages. Closed-loop, real-time spatial and thermal monitoring enables the treatment safer and more accurate. Identifying target nerve is not trivial and the outcome is highly technique-dependent in radiofrequency [25]. MRgFUS treatment is not a technique-dependent procedure and low inter-operator variability is expected. MRgFUS treatment does not cause widespread hypoesthesia which often observed in radiofrequency treatment [25], because MRgFUS treats most peripheral zone of the sensory nerve. On the other hand, there are some obvious disadvantages of MRgFUS. Enormous initial cost of the treatment is most critical. In addition, patients of contraindications for MRI cannot undergo the treatment. Required time for the set up and treatment is also longer than radiofrequency.

This study has some limitations. First, the most important weakness is that it was a case series including small number of patients without control group. Hence, it is difficult to be sure that there were no placebo effects. However, 75% of patients showed successful pain relief along with significant increase of PPTs. Although further study with blinded and randomized controlled trial is required for constructing evidence, our initial results suggested the safety and efficacy of the treatment. Second, the inclusion was restricted most severe medial knee OA because this is a pilot study so that the patients should be salvaged by TKA conversion. Based on this study and the mechanism of pain relief, medial OA in earlier stage or lateral OA might possibly become a candidate for the treatment. Third, this study did not have a long follow-up period. Two patients underwent total knee arthroplasty and one non-responder dropped out one month after the treatment. Long-term effectiveness of MRgFUS treatment including ADL and QOL assessment should also be carried out in a continuing study.

Conclusion

MRgFUS treatment had a potential of rapid and long-lasting pain alleviation without adverse side effects. Significant increase of PPTs on treated area showed successful denervation effect on the nociceptive nerve terminals. MRgFUS is a promising and innovative procedure for noninvasive pain management of knee OA.

Competing interests

The authors have no competing interests to declare in regard to this manuscript.

Authors' contributions

MI was involved in the conception, planning and designing this study, the acquisition of data, analysis and interpretation of data, and writing the manuscript. MI, MK, TU and TGN were involved in planning and designing this study, analysis and interpretation of data, and critical revision of the manuscript for important intellectual content. KM and HN participated in the acquisition of data. YO and TT was involved in planning this study and drafting the manuscript. All authors read and approved the final manuscript.

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トピックス

慢性痛のQOLに与える影響
―尾張旭市で行った大規模住民アンケート調査を基に―

井上　真輔[1)]　牛田　享宏[1,2)]
小林　章雄[3)]　長谷川共美[2,3)]

Abstract: Musculoskeletal disorders are the most common causes of severe long term pain and physical disability, affecting hundreds of millions of people around the world. But, in Japan, there has been a paucity of basic information on the status of chronic musculoskeletal chronic pain. We organized a postal survey designed to quantify and describe the prevalence and distribution of chronic pain in the Japanese community. According to our research, chronic pain of moderate to severe intensity occurs in 17.2%. It was revealed that chronic pain had a significant impact on occupational and social relationships, and it also seriously affect on their psychological and the quality of healthy conditions.

Key words: Chronic pain, Survey, Quality of life

はじめに

運動器の痛みは多くの国民が有する問題であり，慢性化した運動器痛は患者の人生の質（QOL）を下げ，社会生活にも大きな影響をもたらす。超高齢社会を迎えた日本においては，健康寿命に大きな影響を与える運動器慢性痛に関する基礎データは，国民の健康増進や介護予防施策の立案には不可欠である。

平成22年度の厚生労働省の国民生活基礎調査の結果では，男性の自覚症状は「腰痛」が最も多く，次いで「肩こり」であり，女性では「肩こり」が最も多く，「腰痛」，「手足の関節が痛む」がそれに続き，多くの人々が運動器の痛みに悩まされていることがわかる。また，2006年服部ら[3)]が行った運動器痛に関するインターネットを用いた大規模疫学アンケートの結果では，日本人の慢性痛の保有率は約13.4%であり，日本全体の慢性痛保有者は約1,700万人と報告された。さらに2011年にはNakamuraら[5)]が郵送による全国アンケートを行い，その結果，慢性痛の有訴率は15.4%と報告した。両調査によって運動器慢性痛の詳細のほかにも，現状の慢性痛治療の満足度は決して高くはない実情などが浮き彫りとなったものの，人々の生活（QOL）や心理精神状態において慢性痛がどのような影響を及ぼしているかまだ明らか

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にはなっていない。

また，Beckerら[1]は，デンマークのペインセンターに訪れた患者のSF-36（MOS 36-item Short Form Health Survey）を調査した結果，慢性痛患者では全ての下位尺度において，国民標準値を大幅に下回っており，慢性痛がQOLの低下に関連していると報告している。一般住民において，慢性痛の有無がどの程度健康関連QOLに係わっているかについて，我々の調査で詳細に分析した。今回我々は，慢性痛を単なる痛みではなく，多くの人々を悩ませる疾病と捉え，慢性痛の有無が人々のQOLや心理精神状態に及ぼす影響を調査した。

方　法

我々は平成23年11月に，人口8万人の愛知県尾張旭市で郵送方式による慢性痛の疫学調査を行った。調査は市役所の協力を得て，住基ネットよりランダムにサンプリングした20歳以上の6000人にアンケート用紙を郵送した。アンケートの内容は，痛みの有無，程度，持続期間，診断名，運動習慣の有無，QOL，抑うつ等の心理状態についても聴取した。健康関連QOL（Health Related Quality of Life: HRQOL）の指標はEuroQOL-5D日本語版[4]（以下EQ-5D）を使用した。EQ-5Dは5項目3段階の質問からなり，それぞれの回答の組み合わせから最高の健康状態を1，死を0とする効用値に換算することで，QOLを一元的に定量化することができる。SF-36よりも質問数が少なく簡便であるため，大規模調査には有用である。さらに心理的ストレス評価尺度として，の6項目の質問からなるKessler's Psychological Distress Scale日本語版[2]（以下K6）を聴取した。

結　果

回答が得られたのは男性1123人，女性1564人の計2687人で，平均年齢は58歳，回答率は44.5%であった。Numerical rating scale（NRS）で聴取した“痛みの強さ”は平均5.1であった。全体の2.9%は，NRS9もしくは10の極めて強い痛みを有していた。最も痛む場所は，腰，膝，後頸部，肩，臀部の順であった。NRSで5以上，6ヶ月以上続く痛みを慢性痛と定義すると，慢性痛の有訴者率は17.2%であった。EQ-5Dの効用値（以下すべて平均値）は，慢性痛群は

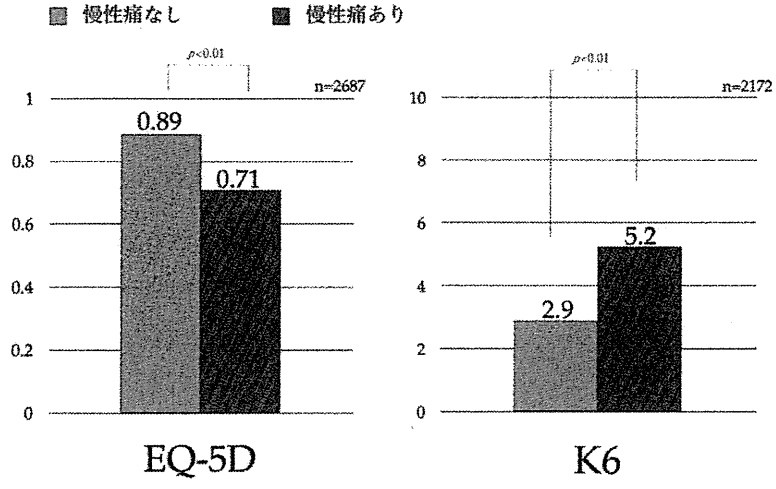

図　慢性痛の有無とQOL及び抑うつとの関連

0.71，慢性痛のない群は0.89で，慢性痛群で有意にQOLが低下していた。しかも，慢性痛群のK6は平均5.2と高く，不安障害のカットオフの5を超えていた（図）。運動習慣のない群では運動習慣の有る群と比べて，慢性痛の有訴率が高く，QOLも低かった。また，QOLと抑うつのスコアが最も低かった痛みの診断名は，脳卒中後の痛み，脊椎手術後の痛み，人工関節手術後の痛みであり，特に手術後の疼痛は人々の生活への影響が大きいことが示唆された。

考　察

今回の調査では，慢性痛の定義を「NRSで5以上かつ6ヶ月以上続く痛み」として算出した慢性痛有訴者率は17.2%であった。前述した本邦における報告や欧州で行われた調査も総合して勘案すると，我が国においては約2000万人が程度の強い慢性痛に悩んでいると概算される。

痛みという現象は，単に生物的な侵害感覚ではなく，心理的もしくは社会的要因に修飾される多因性の情動である。長く続くつらい痛みは人を患者へと変え，患者の家族や周囲の人間にも暗い影を落とす。我が国の慢性痛患者においては明らかにQOLが低下しており，また抑うつの指標も高く，国民が明るく健康的な生活を送る社会を作るためには，今回の調査で把握された慢性痛の実態に基づいた包括的な慢性痛対策の必要性が求められる。また，様々な原因の慢性痛の中でも，術後の慢性疼痛や脳梗塞後の神経障害性疼痛は心理的負荷が極めて大きいことが示唆された。このことからは同じ慢性痛でも，その原因によって大きく障害度は異なることが読み取れる。医療者は，患者背景も踏まえて慢性痛の原因疾患を探り，時には痛みを取り去ることに執心せず，心理的なケアや生活習慣のアドバイスなど患者の生活の質の向上を目的とした集学的な治療を心がけることも肝要である。

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集学的痛みセンターにおける診療の課題と展望

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集学的痛みセンターにおける診療の課題と展望

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要　旨

難治性慢性疼痛の治療に有効な集学的治療が，一部で，薬物療法やブロックが効かなければ，脊髄刺激電極などの治療法を併用するなどといった単純なものと誤解されているところがある．痛みは，生物学的，心理学的，社会学的要因が複雑に絡み合って生じる症状であり，生物学的，心理学的，社会学的に関する専門的知識を有した医療従事者が同時に治療介入しなければならない．これが集学的治療である．集学的に難治性疼痛を診療するには，かなりのマンパワーと時間が必要となり，日本の医療制度と診療報酬制度が集学的治療の妨げになっている．ここでは，現在ある課題と展望について述べる．

（ペインクリニック 34：753-759，2013）

キーワード：難治性慢性疼痛，集学的治療，痛みセンター

はじめに

難治性慢性疼痛の治療に集学的治療が有効な治療法であることは，欧米では半世紀前より認識されてきており，日本においても，近年，知られてきている．しかし，集学的治療というものがどのようなものであるかに関しては，多くの医療者において誤解されている現状がある．まず，集学的治療が必要と認識されるに至った背景について述べる．

日常生活における痛みの経験はほとんどが一過性のもので，急性の痛みでは，たいていの場合，投薬を含めた治療で治まる．しかし，慢性の痛みでは，がんなど特殊な病気によるものを除いては，ほとんどが原因のわからないものであり，仮に原因がわかっても治療に難渋することが多い．

欧米ではおおよそ50年前に痛み専門の治療機関が設立された．日本でも，1962年に最初のペインクリニックが設立された[1]．当初，1641年にデカルトの提唱した「心身二元論」に基づき，体と心を切り離して考える概念により，医師や患者は，痛みは病気やけがに起因し，それらは検査で検出できるはずだと信じて，痛みは身体的なものと考えた生物学医学的モデルを基にしていたため（**図1**），ペインクリニックでは局所麻酔的な治療や神経ブロックを主体に治療が行われていた．1970年代に，このような方法では治すことのできない痛みの症候群が存在することが明らかになり始め，従来の生物学医学的モデルは，器質的要因を探すことが医師の責務であり，心理社会的要因により生じる機能不全を考慮しないものとして異議を唱え

〈Special Article〉 Problems and prospects in the pain clinic practice in Japan
Problems and prospects in multidisciplinary pain center in Japan
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図1　生物学医学的モデルにおける痛みの治療

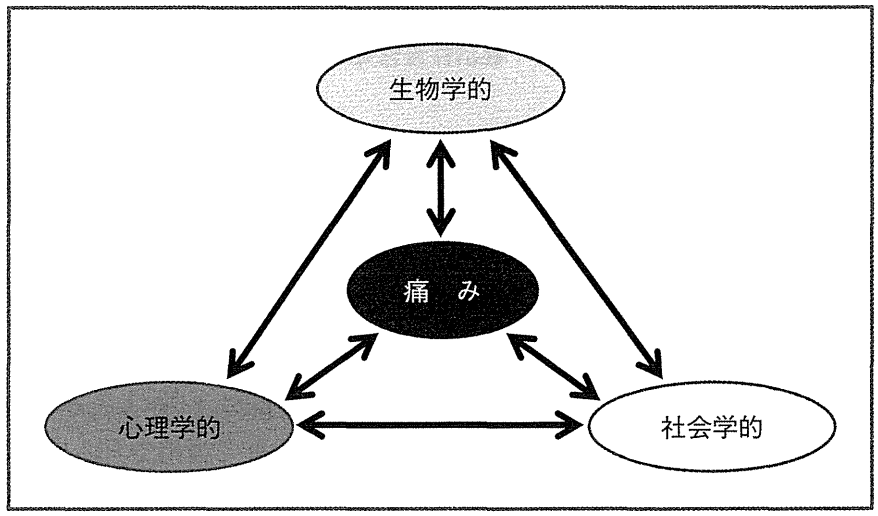

図2　痛みの生物心理社会モデル

られた．ここで，生物心理社会モデルが新たに提唱された[2]．このモデルでは，生物学的，心理学的，社会学的問題を，ちょうど筋骨格系や心血管系などと同じように全身のシステムの一部とみなし，心と体は切り離して考えられるものではないとしている（**図2**）．痛みは，生物学的，心理学的，社会学的要因が複雑に絡み合って生じる症状であり，すべての人に継続的に影響を与える．

したがって，難治性慢性疼痛の治療において，薬物療法や通常の神経ブロックが効かなければ，脊髄刺激電極植え込みによる脊髄刺激，高周波熱凝固や高周波パルス療法を併用するなどといったものが集学的治療になり得るのではなく，患者の生物学的，心理学的，社会学的要因に関する専門的知識を有した医療従事者が，同時に評価，議論，治療介入することこそが集学的疼痛治療となり，これを有機的に行っていく

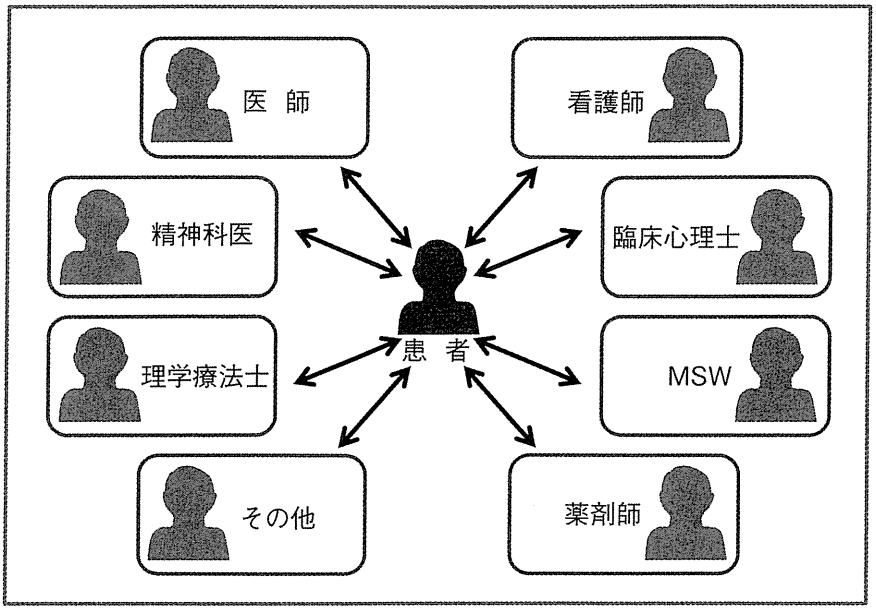

図３　集学的痛みセンターチーム（マルチディシプリナリー）

ユニットが集学的痛みセンターとなる．

１．集学的痛みセンターチーム（図３）

欧米の痛みセンターでは，基本的に医師，看護師，理学療法士，心理士などが主なチームのメンバーである．われわれは大学研究機関の一部であるので，すべてのスタッフが痛みの基礎と臨床研究を行っている．このように，痛みに対し多角的に取り組んでいる施設が「痛みセンター」と呼ばれ，医師が単一モードで痛みに対して取り組む「ペインクリニック」とは区別される[3]．

１）学際的痛みセンターチーム構成員と役割

①医師（整形外科医，麻酔科医，心療内科医）

ⅰ）病状の診断
ⅱ）検査
ⅲ）薬物処方
ⅳ）神経ブロック，トリガーポイント注射などの処置
ⅴ）東洋医学的な鍼灸治療と漢方薬処方
ⅵ）患者教育

②看護師

ⅰ）バイタルサインや病歴聴取
ⅱ）検査，処置的治療の介助
ⅲ）患者の悩みの傾聴
ⅳ）ライフスタイルの教育と指導

③理学療法士

ⅰ）筋骨格系の検査と評価
ⅱ）筋骨格系のコンディショニング
ⅲ）ストレッチングなどセルフケアの指導
ⅳ）理学療法的な教育

④臨床心理士

ⅰ）心理社会的評価
ⅱ）精神疾患の評価と診断
ⅲ）カウンセリング
ⅳ）患者教育

⑤薬剤師

ⅰ）多薬併用など薬物処方の評価
ⅱ）薬物に関する医師への適切な助言
ⅲ）薬物教育

表1　病院長に対するアンケート調査結果

A．慢性痛は，痛みが長く続くことによる不安・抑うつなどの精神心理的要因，家族や会社での人間関係，経済問題などの社会的要因が複雑に絡む頻度が高いことをご存知ですか．（答えは1つのみ）

はい	57	95.0%
いいえ	2	3.3%
未記入	1	1.7%

B．そのような心理社会的要因を含む慢性痛を解決するためには，単独の診療科がそれぞれに対処するだけでは難しく，複数の診療科が同じ場所で協議して，共通の理念を持って治療に当たる集学的な疼痛治療ユニット（痛みセンター）が有効であるとされています．米国，スウェーデンをはじめとして，広く欧米諸国において，そのような集学的痛みセンターの整備が進んでいることをご存知ですか．（答えは1つのみ）

知っていた	31	51.7%
知らなかった	27	45.0%
未記入	2	3.3%

C．慢性痛患者さんを特化して扱うチームを創ることは，病院全体の診療効率を上げることにつながると考えますか．（答えは1つのみ）

はい	52	86.7%
いいえ	6	10.0%
未記入	2	3.3%

D．厚生労働省の“慢性の痛みに関する検討会”で，わが国における複数の診療科とコメディカルを含めた集学的な痛み治療体制の必要性とチーム医療の推進が指摘されております．そこで，現在の状況で貴院（貴学）において，そのような集学的な疼痛治療ユニット（兼務も可）を開設することは可能ですか．（答えは1つのみ）

可能である	39	65.0%
不可能である	19	31.7%
未記入	2	3.3%

E．集学的な疼痛治療ユニットを開設するためには，どんな問題を解決する必要があると考えますか．（答えは1つのみ）

お金の問題（開設しても収入に結びつかない）	40	66.7%
人の問題（やってくれる人材がいない）	52	86.7%
物の問題（開設するスペースがない）	29	48.3%
集学的な疼痛治療ユニットの必要性を感じない	3	5.0%
その他	4	6.7%

2．集学的痛みセンターにおける診療の課題

ここで，全国の大学病院の病院長に宛ててわれわれが行ったアンケート調査の結果を示す．全国80の大学病院の中で60の大学病院より返事を得た．**表1A**に示すように，慢性疼痛が，単に器質的要因だけではなく，精神心理的要因や社会的要因が複雑に絡んだ問題であることは，多くの病院の病院長には理解されていることがわかる．さらに，複雑な因子が絡んだ慢性

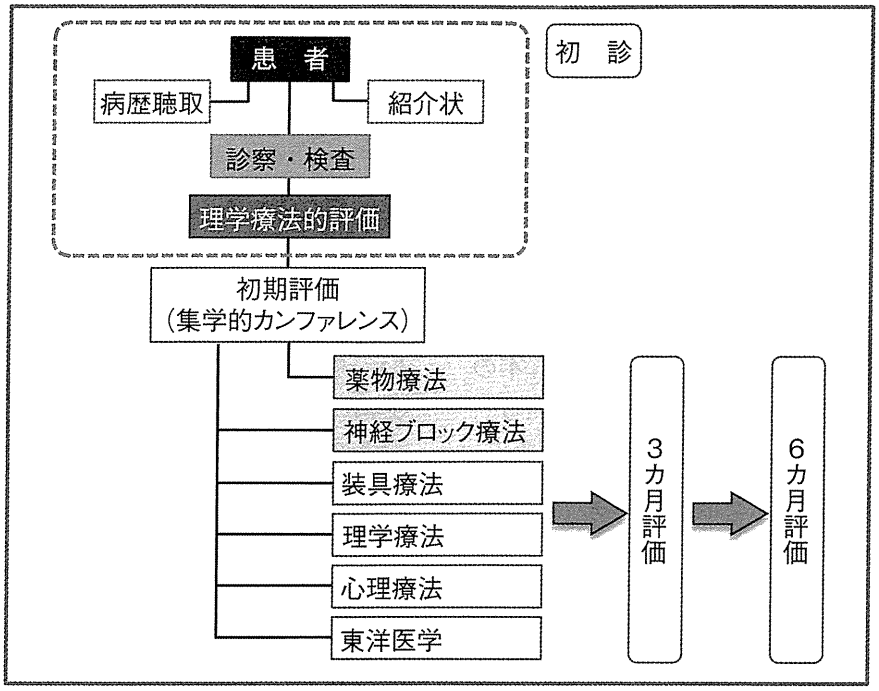

図4　治療の流れ

疼痛を治療するには，単独の診療科ではなく，複数の診療科が共同で治療介入する必要があり，そのようなことができる施設がすでに欧米では整備が進んでいることをすでに知っていた病院長が半数にも及ぶことがわかる（表1B）．また，集学的痛みセンター設置で診療効率を上げることができることも理解している病院長はかなりの人数に上る（表1C）．

慢性疼痛を有する患者の診療では，医師がしっかりと患者の話を聞き，触れ，痛みや訴えをできる限り理解しようとすることが治療の原則である．そのためには，一定の時間を患者との問診に割くことが必要不可欠であるが，現在の医療制度では入院・外来を問わず，注射や投薬などの処置を行わないと診療報酬につながらないという大きな問題が背景にあるため，この診療原則がないがしろにされる傾向にある．したがって，われわれのような痛みセンターで集学的治療を円滑に運営するために，初診においては，まずはじめに詳細な問診を看護師に採ってもらい，紹介状をも併せて，適切な検査を追加して，さらに筋骨格系の評価を理学療法士に行ってもらった後に（図4），コメディカルを含めた各専門分野間での話し合いによる情報交換の場が必要となる．場合によっては，次回の受診で痛みセンターに属する精神科医や臨床心理士の評価も行う．われわれの施設では週2回のカンファレンスを行い，チーム内で各医療従事者が積極的に発言し，議論し，治療方針などを検討しており，“チームとして取り組んでいく”という認識にも良い影響を与えている．このように，集学的に難治性疼痛を診療するには，かなりのマンパワーと時間が必要となる（図4）．

各大学病院において集学的痛みセンター開設は可能であるか，のアンケートに関しては，3分の2もの大学病院の病院長が可能であると答えている（表1D）．しかし，開設するに当たり問題となるのは，やはり金銭的な問題，マンパワー的な問題や開設する場所の問題などが大きい（表1E）．実際，われわれが知る限りでは，

集学的治療として，麻酔科医，整形外科医，精神科医，看護師，理学療法士，臨床心理士が一堂に会して，議論し，治療介入できている施設は，全国で10施設にも満たない．日本の保険制度上，科別の診療コストの制度は集学的治療チーム編成の弊害になり，日本で集学的痛みケア施設の設立を遅らせる原因にもなっている．診療科の壁の問題だけではなく，医師－コメディカル間の職種の壁を取り除くことも日本の医療体制ではかなり難しいものとなっている．実際，われわれの施設でも，病院予算の関係上，一部のスタッフは他科との兼任や非常勤対応であるという問題点もあるが，さらに工夫を重ね，システム構築を今後も模索していく必要があるものと考えている．

3．集学的痛みセンターにおける診療の展望

前述したように，現時点で，集学的な医療を実践するには，日本の医療保険システム上，採算性が低くなる．そのため，慢性難治性疼痛に集学的治療を実践するには高いハードルが存在している．しかし，今後，医療費削減や治療効率向上のため，欧米と同じような集学的痛みセンター開設が各地方の基幹病院で必要であることは想像に難くない．実際，厚生労働省は2009年に有識者を集め，『慢性の痛みに関する検討会』を開催し，慢性疼痛に対する治療に集学的痛みセンターに必要性や治療対価の問題について本格的に検討が始まり，現在も行われている[4]．

しかし，利益を度外視して，各医療施設が経済的に大きな負担になる程のマンパワーを必要とする集学的痛みセンターを設立することには無理がある．そこで，集学的疼痛治療において，保健医療における診療報酬の算定法の改革が大切で，集学的治療を行うことで診療報酬加算が採れる制度の確立が必要と考える．そこで，モデルとなり得るものは，緩和ケア診療加算ではないかと考える．この加算では，専従2名と専任1名のコアスタッフの任命が必要である[5]．ここから考えると，集学的慢性疼痛治療に関する保険診療加算では，生物学的要因について治療介入する医師（麻酔科医，整形外科医）または理学療法士，また，心理学的，社会学的問題に治療介入する精神科医または臨床心理士が，専任でチーム構成されるように任命されるといったような施設基準になるのではないかと考える．

しかし，緩和ケア診療加算に関する多くの報告で，年間収入が人件費にも満たないことが問題である[5,6]．また，実際に加算を算定できるように緩和チームを整備している施設は日本全国の中でごくわずかである．これは，人材不足の原因も考えられるが，前述したように，チームを編成しても，多くの施設では人件費を満たすこともできないため，チーム編成に消極的であるためと考える．私見ではあるが，集学的痛みセンターを開設するに当たっては，各都道府県で人口密度の隔たりもあるので，できれば各大学病院に1施設が理想かもしれない．そこで，国は各大学病院が開設に消極的にならない程度の収入が得られるように，診療報酬加算のシステムを作る必要があると考える．

ま と め

難治性慢性疼痛における集学的治療は，薬物療法や通常の神経ブロックが効かなければ，そのほかの治療法として脊髄刺激電極植え込みによる脊髄刺激療法，高周波熱凝固術や高周波パルス神経ブロックを併用するなどといった単純なものではなく，生物学的，心理学的，社会学的要因が複雑に絡み合って生じる疼痛に，生物学的，心理学的，社会学的に関する専門的知識を有した医療従事者が同時に評価，議論，治療介入するものである．現在の医療制度や保険診療報酬制度のため，マンパワーと時間をかなり

必要とするこのような集学的治療を行っていくことは，かなり難しい状況であり，実際，全国でも実践できている施設は10施設にも満たない．難治性慢性疼痛に集学的治療が必要であり，集学的痛みセンターの開設が急がれるべきことと認識されてきている現在，国の医療制度と保険診療報酬制度の早急な改革に期待したい．

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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]

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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

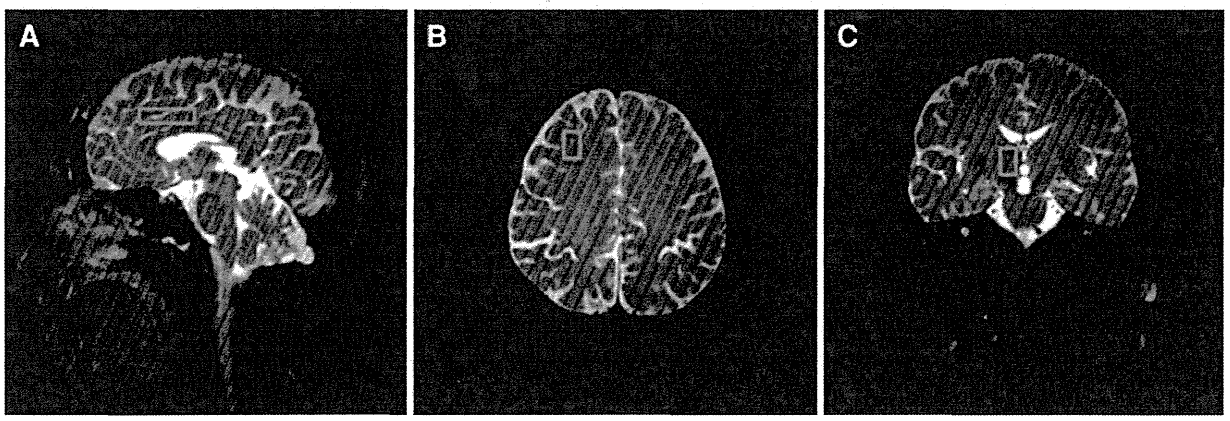

Fig. 1 Location of the spectroscopic voxel in the brain. **a** Anterior cingulated cortex (ACC). **b** Prefrontal cortex (PFC). **c** Thalamus

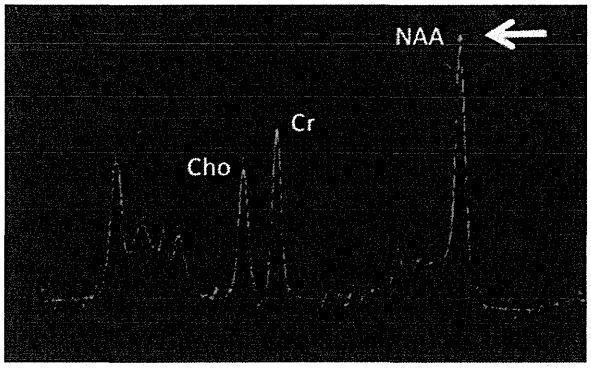

Fig. 2 Proton localized spectra. *NAA N*-acetyl aspartate, *Cr* creatine/phosphocreatine complex, *Cho* choline

Table 2 NAA/Cr compared between subjects and control

	Subjects (mean ± SD)	Control (mean ± SD)	*p* value
R ACC	1.313 ± 0.189	1.242 ± 0.134	0.337
L ACC	1.169 ± 0.478	1.355 + 0.077	0.63
R PFC	1.609 ± 0.252	1.651 ± 0.136	0.873
L PFC	1.526 ± 0.154	1.560 ± 0.136	0.688
R thalamus	1.292 ± 0.062	1.536 ± 0.172	0.025
L thalamus	1.328 ± 0.103	1.439 ± 0.141	0.15

R right, *L* left, *ACC* anterior circulated cortex, *PFC* prefrontal cortex

Table 3 NAA/Cho compared between subjects and control

	Subjects (mean ± SD)	Control (mean ± SD)	*p* value
R ACC	1.473 ± 0.244	1.476 ± 0.224	1
L ACC	1.277 ± 0.548	1.497 ± 0.178	0.631
R PFC	2.488 ± 0.465	2.498 ± 0.238	0.522
L PFC	2.274 ± 0.548	2.218 ± 0.264	1
R thalamus	1.586 ± 0.097	1.919 ± 0.163	0.006
L thalamus	1.738 ± 0.239	1.783 ± 0.161	0.81

R right, *L* left, *ACC* anterior cingulated cortex, *PFC* prefrontal cortex

Results

On the psychiatric states evaluated by the BS-POP, five of six patients had normal scores, with one patient having an abnormal borderline score (11 points). Therefore, we concluded that these patients had no severe psychiatric problems.

On the NAA/Cr, there were no statistically significant differences between the two groups in the bilateral ACC, PFC and left thalamus. However, in the right thalamus (contralateral side to the symptom), the NAA/Cr in the subjects (1.29 ± 0.62) was statistically significantly lower compared with controls (1.54 ± 0.17; $p < 0.05$) (Table 2). On the NAA/Cho, there were also no statistically significant differences between the two groups in the bilateral ACC, PFC and left thalamus. However, in the right thalamus (contralateral side to the symptom), the NAA/Cho in the subjects (1.59 ± 0.097) was statistically significantly lower compared with controls (1.92 ± 0.16; $p < 0.005$) (Table 3). All NAA/Cr and NAA/Cho data for the thalamus are shown in Table 4. When the differences between the right and left side of the NAA/Cr and NAA/Cho in the thalamus were compared between the subjects and the control group, only the NAA/Cr ratio was statistically significant different ($p < 0.05$).

When focused on the right thalamus, there were statistically significant correlations between the NRS and NAA values (Fig. 3). In the ACC and PFC, there were no significant correlations between the NRS and NAA values.

Table 4 NAA/Cr and NAA/Cho in the thalamus

Subjects or control	NAA/Cr in the rt. thalamus	NAA/Cr in the lt. thalamus	NAA/Cho in the rt. thalamus	NAA/Cho in the lt. thalamus
Subject 1	1.34	1.25	1.6	2.03
Subject 2	1.336	1.301	1.721	1.779
Subject 3	1.322	1.231	1.639	1.437
Subject 4	1.19	1.42	1.52	1.79
Subject 5	1.24	1.49	1.44	1.92
Subject 6	1.323	1.278	1.596	1.471
Control 1	1.67	1.35	2.02	1.92
Control 2	1.3	1.27	1.65	1.59
Control 3	1.51	1.46	1.99	1.98
Control 4	1.79	1.66	2.11	1.67
Control 5	1.46	1.53	1.92	1.87
Control 6	1.484	1.364	1.826	1.666

Discussion

This study demonstrated that the patients with unilateral pain (LBP and/or sciatica) due to lumbar spine diseases with shorter duration (within 12 months) of pain and without severe psychiatric conditions showed decreases in the NAA/Cr and NAA/Cho in the thalamus on the contralateral side from the symptom. There were statistically significant correlations between NRS and NAA values. Lumbar pain can possibly be assessed indirectly by analyzing the decrease in the NAA concentration in the thalamus.

Recent pain studies using fMRI [6–8], positron emission tomography (PET) [18, 19] and single-photon emission computed tomography (SPECT) [20, 21] have shown that functional changes mainly occurred in the ACC, PFC and thalamus in patients with chronic pain. PET and fMRI studies in the healthy subjects demonstrated that acute pain activated the primary and secondary somatosensory cortex (S1 and S2), insular cortex, ACC, PFC and thalamus [22]. These areas and the basal ganglia, cerebellum, amygdala, hippocampus and regions within the parietal and temporal cortices are often called the "pain matrix." The matrix can be thought of as having lateral components (sensory-discriminatory, involving areas such as the primary and secondary somatosensory cortices, thalamus and posterior parts of the insula) and medial components (affective-cognitive-evaluative, involving areas such as the anterior

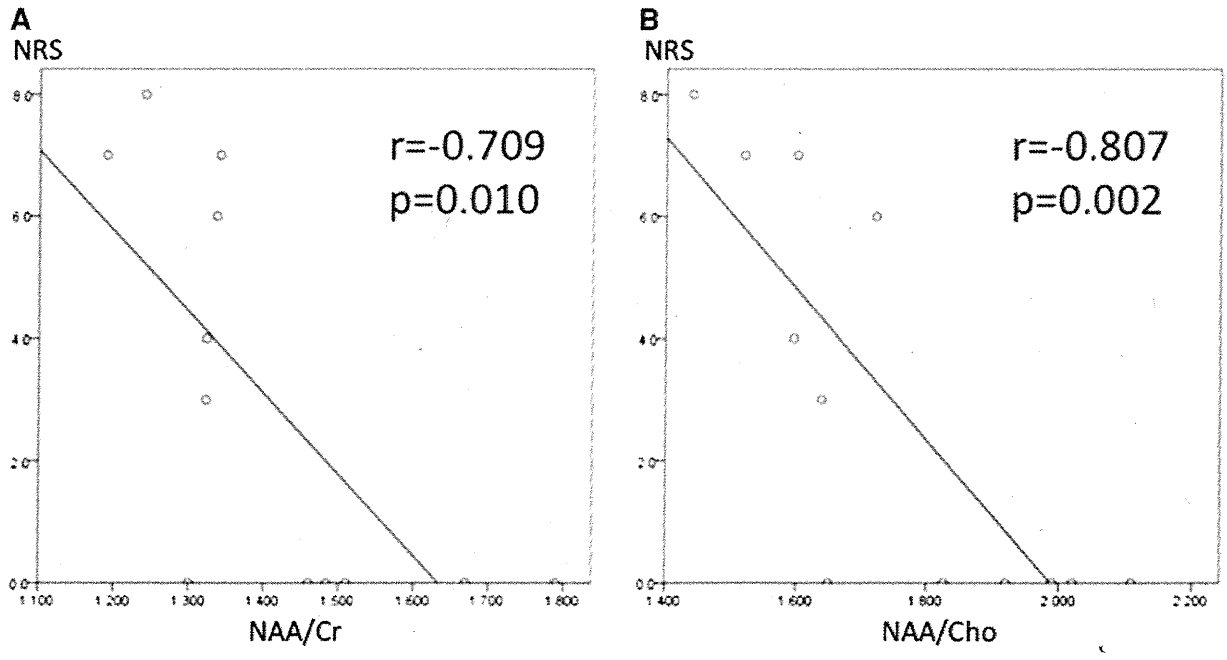

Fig. 3 Correlation between the NRS and NAA in the thalamus. **a** Correlation between the NRS and NAA/Cr. **b** Correlation between the NRS and NAA/Cho. *NRS* Numerical rating scale for pain, *NAA* *N*-acetyl aspartate, *Cr* creatine/phosphocreatine complex, *Cho* choline

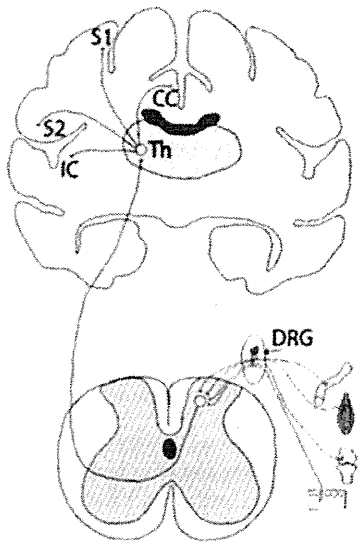

Fig. 4 Pain pathway. Every sensory system except for the olfactory system includes a thalamic nucleus that receives sensory signals and sends them to the associated primary cortical area. *S1* Primary somatosensory cortex, *S2* secondary somatosensory cortex, *IC* insular cortex (reproduced from [24] with permission)

parts of the insula, ACC and PFC) [23]. The current study showed NAA reduction only in the contralateral thalamus. This finding may suggest that the subjects in this study had little affective-cognitive-evaluative factor associated with their pain. However, the "pain matrix" is not a definitive entity because different brain regions play a more or less active role depending on the precise interplay of the factors involved in influencing pain perception, for example, cognition and mood.

In the current study, we used MRS for evaluation of lumbar pain (LBP and sciatica). An exact correlation between MRS and other brain imaging is still uncertain [22]. The NAA is localized within neurons and involved in synaptic processes. It has been observed to decrease in various conditions involving neuronal cell damage and loss and is therefore thought to be a neuronal and axonal marker [11, 22, 24]. CLBP is a multifactorial, pathological condition involving psychiatric problems, which may influence the results of NAA concentration [25]. In the current study, pain duration was less than 12 months, and the BS-POP was essentially normal. Therefore, the results of this study may show pain due to lumbar spine diseases without influence of psychiatric problems.

There is some variability in MRS results. It has been reported that the NAA concentration and NAA/Cho were higher in the left thalamus by 21.9 and 20 %, respectively, in healthy subjects [26]. However, the results of the current study showed lower NAA/Cr and NAA/Cho in the left thalamus in the control group (Table 4). The cause is not clear. Side matching in the same subjects may be important for proton MRS studies. All of the subjects in the current preliminary report had left side pain. Regarding the relationship between age and NAA, Charles et al. [27] reported that the choline, creatine and NAA were lower in older subjects in the voxel representing cortical and subcortical gray matter. Recent studies by Grachev et al. [28, 29] demonstrated that there was no evidence for NAA correlation strength differences in the thalamus, insula, orbital frontal cortex and sensorimotor cortex between the young-aged group and middle-aged group. Regarding the relationship between gender and NAA, Charles et al. [27] and Nagae-Poetscher et al. [26] reported that there were no differences between males and females. Therefore, age matching may be more important than gender matching for comparative studies of disease states using proton MRS.

The thalamus plays an important role in the pain pathway. Every sensory system except for the olfactory system includes a thalamic nucleus that receives sensory signals and sends them to the associated primary cortical area (Fig. 4) [30]. The relation between NAA concentration in the thalamus and pain has been previously reported. Pattany and colleagues [31] showed that the NAA concentration was negatively correlated with pain intensity in patients with chronic neuropathic pain after spinal cord injury. Fukui and colleagues [32] showed a decrease in the NAA concentration on the contralateral side in seven of nine neuropathic pain patients. Our study showed similar results using subjects with a shorter duration of pain. The NAA concentration in the thalamus may decrease during the acute stage of pain. However, the relationship among NAA changes, duration of pain and therapeutic efficacy was not clarified in the current study. A decrease in thalamic perfusion has been reported in patients with chronic pain using SPECT [20, 21]. If effective treatment is not given and the NAA reduction lasts for a long time, a chronic pain condition may develop in patients with severe acute pain. Further studies are needed to clarify these important points.

The current study has several limitations. The number of patients was very small. Strict age matching and gender matching were not performed. The symptom duration was short. The MRI instrument had no linear combination model (LC model) software that could measure the absolute concentration of NAA [33, 34]. We analyzed the NAA concentration in only three brain regions (ACC, PFC and thalamus). Further studies in more patients with various pain conditions are needed. In conclusion, lumbar pain in patients with shorter durations of pain and without severe psychiatric conditions may be objectively assessed indirectly by analyzing the decrease in the NAA concentration in the thalamus.

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Conflict of interest No benefits in any form have been or will be received from a commercial party related directly or indirectly to the subject of this manuscript.

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