min before compression of EDL muscle 2 days after ECC, and white columns show those in the control group that received saline instead of morphine. Number of animals was 5 for the morphine group, and 6 for the control group. Note that c-Fos immunoreactivity was clearly suppressed in the morphine-treated group (**p<0.01, Mann-Whitney test).

Fig. 1

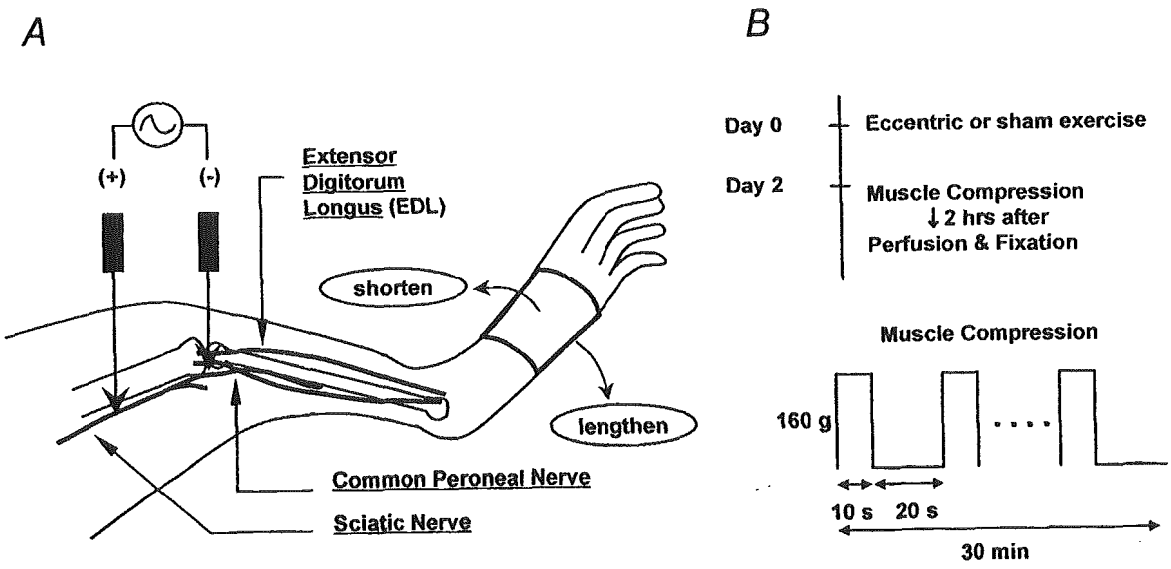


Fig. 2

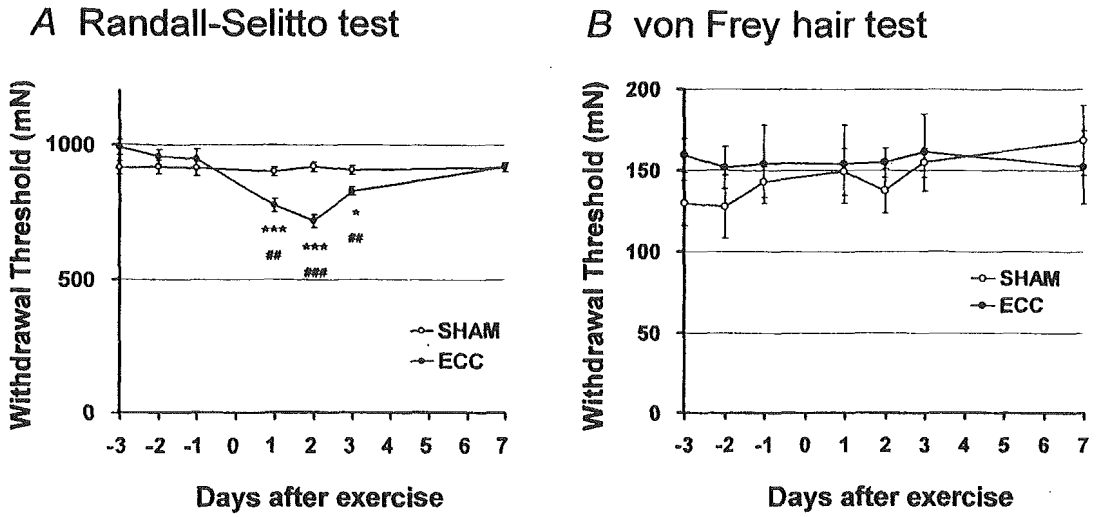


Fig. 3

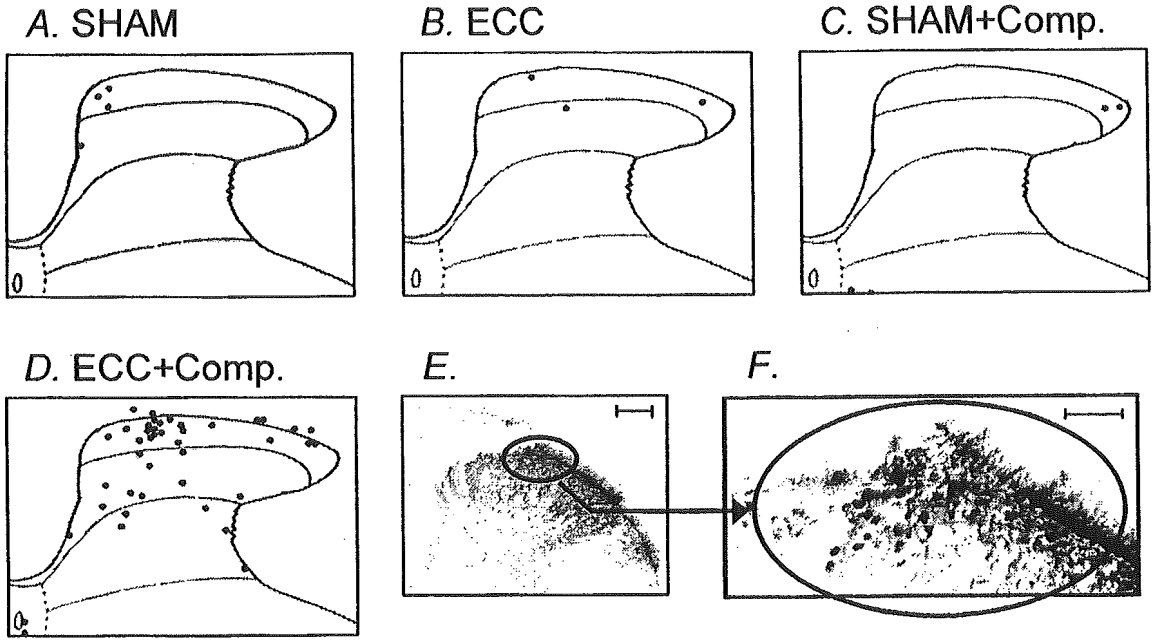

A. SHAM
B. ECC
C. SHAM+Comp.
D. ECC+Comp.
E.
F.

Fig. 4

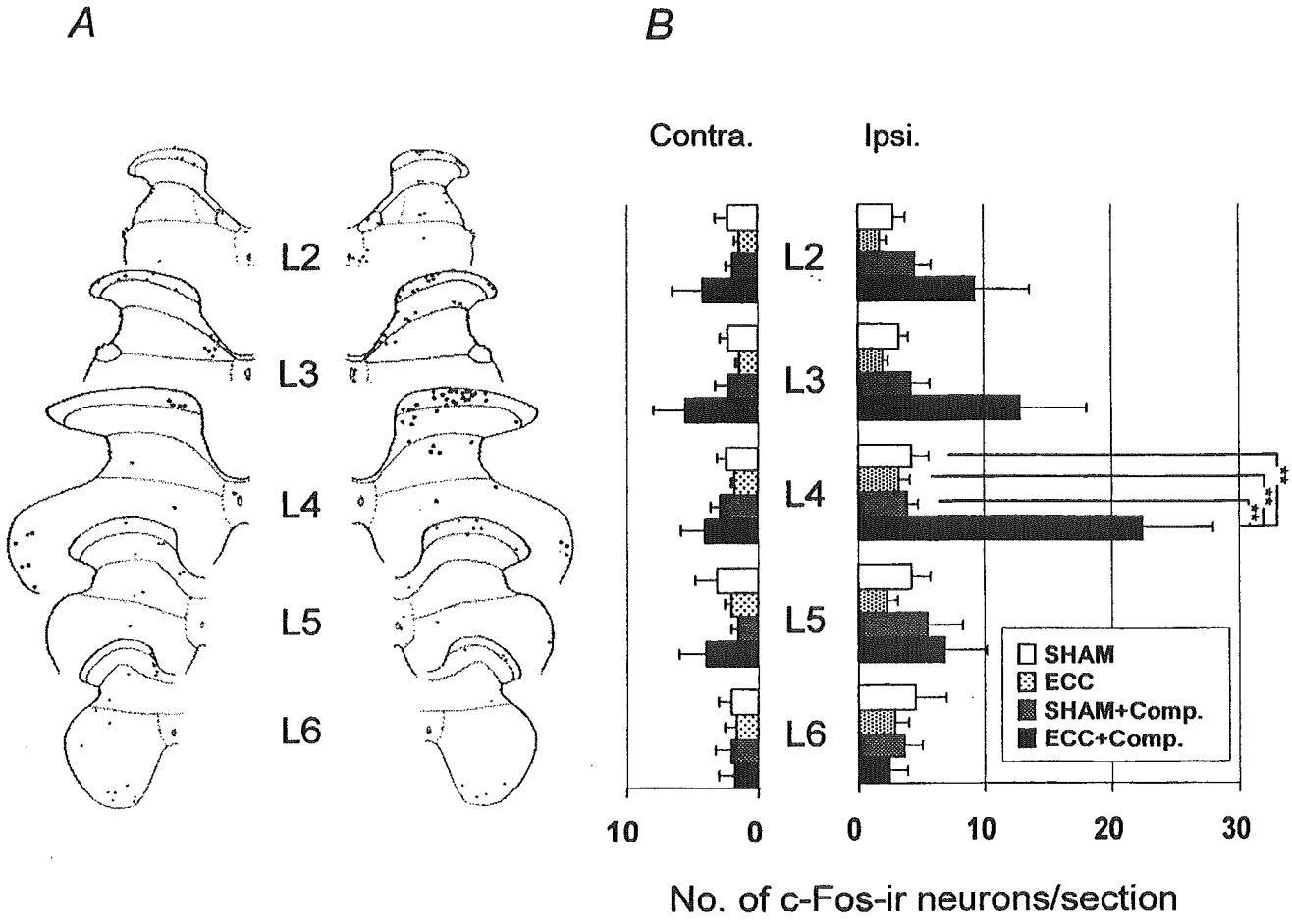
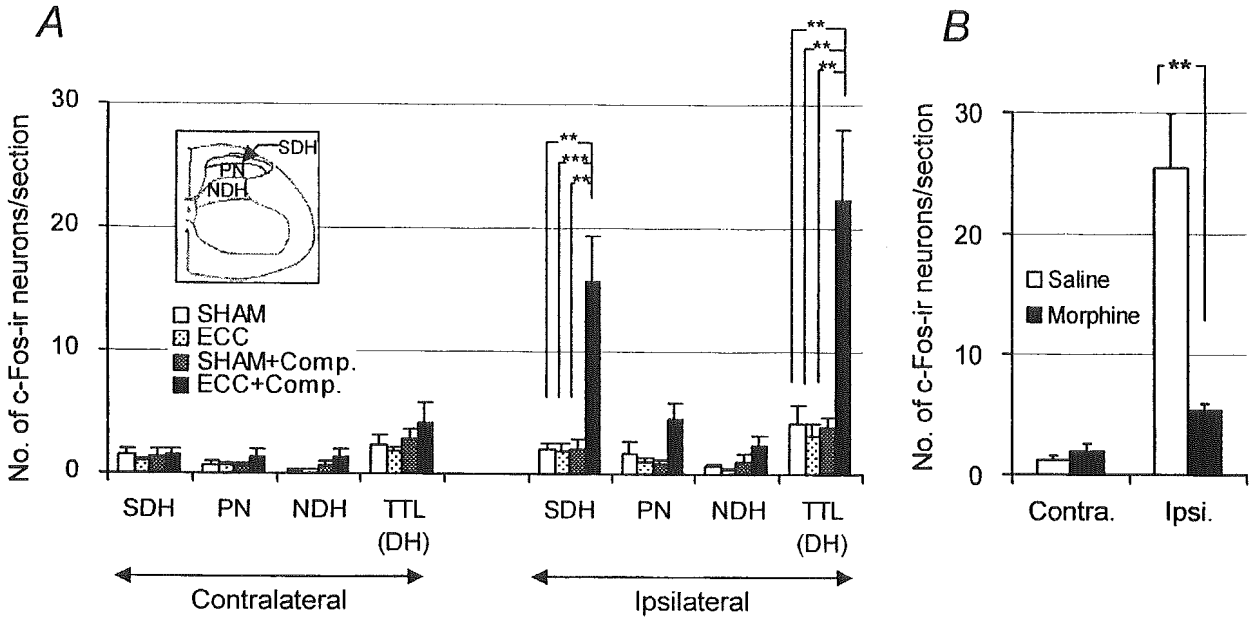

A
B
L2
L3
L4
L5
L6
Contra.
Ipsi.
SHAM
ECC
SHAM+Comp.
ECC+Comp.
10
0
0
10
20
30
No. of c-Fos-ir neurons/section

Fig. 5


A
B
No. of c-Fos-ir neurons/section
30
20
10
0
SDH
PN
NDH
SHAM
ECC
SHAM+Comp.
ECC+Comp.
SDH
PN
NDH
TTL (DH)
Contralateral
Ipsilateral
**
***
Saline
Morphine
Contra.
Ipsi.

ELSEVIER

Neuroscience Letters 354 (2004) 46–49

Neuroscience Letters

www.elsevier.com/locate/neulet

Artificially produced meteorological changes aggravate pain in adjuvant-induced arthritic rats

Jun Sato*, Morihiko Aoyama, Masahiro Yamazaki, Satoshi Okumura, Ken Takahashi, Megumi Funakubo, Kazue Mizumura

Department of Neural Regulation, Research Institute of Environmental Medicine, Nagoya University, Furo-cho, Chikusa-ku, Nagoya 464-8601, Japan

Received 18 August 2003; received in revised form 24 September 2003; accepted 25 September 2003

Abstract

To examine the effects of change in meteorological parameters on pain-related behaviors in a simulated arthritic condition, rats with an injection of complete Freund's adjuvant into the tibio-tarsal joint were exposed to low barometric pressure (20 mmHg below the natural atmospheric pressure) and low ambient temperature (7 °C lower than 22 °C) in a climate-controlled room. When the arthritic rats were exposed to these environments, the already increased number of hindpaw withdrawals in response to noxious mechanical stimulation (hyperalgesia) was further increased, and a hindpaw withdrawal response to innocuous mechanical stimulation (allodynia) began to occur. Such exposures did not influence any of the pain-related behaviors of the control rats. These results show that lowering barometric pressure and ambient temperature within the range of natural environmental fluctuation intensify pain in arthritic rats.

Keywords: Rheumatic pain; Mechanical allodynia; Mechanical hyperalgesia; Weather; Monoarthritis; Rat

Several clinical studies have demonstrated a consistent relation between changes in meteorological factors and pain intensity in subjects with chronic pain (for review, see [6]). Other studies, however, failed to find a significant relationship between pain and weather change [4,9]. These contradictory results led us to conduct a behavioral animal study to determine whether artificial changes in meteorological factors aggravate pain-related behaviors in rats rendered neuropathic by a chronic constriction injury (CCI) to the sciatic nerve. Our studies indicated that exposures to low barometric pressure (LP, 20 mmHg lower than atmospheric pressure) and low ambient temperature (LT, 7 °C lower than 22 °C) augmented spontaneous pain, mechanical allodynia and hyperalgesia shown in the hindpaw skin of CCI rats [11,12,15]. Additionally, sympathectomy eliminated the effects of LP but not LT, suggesting that sympathetic nerve activity makes an important contribution to the LP effect.

A positive relationship between weather and rheumatic pain intensity in humans has been often reported [1,7,8,16]. To date, however, there have been no controlled animal studies examining the mechanism that causes such weather-related aggravation of rheumatic pain. In the present study, therefore, we investigated whether lowering the barometric pressure and ambient temperature within the range of natural environmental fluctuation, simulated in a climate-controlled room, aggravates mechanical allodynia and hyperalgesia in adjuvant arthritis of rats. This condition has many features common with human rheumatoid arthritis and often is used for the study of inflammatory pain mechanisms.

Sixteen adult male Sprague–Dawley rats (250–260 g) were used in this study. Monoarthritis was induced according to the method developed by Butler et al. [3]. Eight rats received an injection of 0.05 ml of complete Freund's adjuvant (CFA) solution into the left tibio-tarsal joint (experimental rats) under sodium pentobarbital anesthesia (55 mg/kg, i.p.), while the control rats ($n = 8$) were injected with 0.05 ml of saline. Three days after inoculation of the CFA, the rats developed inflammation (redness and swelling) in the tibio-tarsal joint to which it was injected and the adjacent skin. Despite such local inflammation, the general condition of these animals (e.g. body weight gain) was not affected. The animals were kept

* Corresponding author. Tel.: +81-52-789-3862; fax: +81-52-789-3889.
E-mail address: jun@riem.nagoya-u.ac.jp (J. Sato).

0304-3940/03/$ - see front matter © 2003 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.neulet.2003.09.057

in a temperature-controlled room (22 ± 1 °C) on a 12:12-h alternating light/dark cycle. To minimize the discomfort of animals, rats that developed signs of inflammation were isolated into separate cages. Water and food were provided ad libitum. Before LP or LT exposure, the animals were kept in the climate-controlled room (ambient temperature 22 °C; relative humidity 50%) for 60–90 min. The rats were exposed to LP by decreasing the barometric pressure of the room below that of the atmospheric pressure by 20 mmHg, which is the change often observed when a low-pressure system passes. This was done over 8 min. The pressure was maintained at this level for 44 min, and then returned to the baseline pressure over 8 min. Ambient temperature was kept at 22 °C and relative humidity at 50%. For LT exposure, the ambient temperature was decreased by 7 °C, which is a typical daily drop in temperature in Japan. This temperature drop, from 22 °C to 15 °C, was made over 13 min. The temperature was then maintained at 15 °C for 44 min, and returned to the baseline temperature over another 13 min. Relative humidity was kept at 50% and barometric pressure was the natural barometric pressure. A behavioral test (described below) was carried out four times; 60 min before exposure, twice at the lowest pressure or temperature (just after and 35 min after reaching the pre-set low pressure or temperature level), and 60 min after exposure.

Pain-related behaviors to mechanical stimulation were measured with self-made von Frey hairs (VFHs, diameter: 0.5 mm, bending forces 34.3, 92.2, 197.2 mN). The rats were placed individually on an elevated grid floor and the VFHs were applied to different parts of the plantar surface at the heel. Each VFH was applied ten times (once every 2–3 s) to the injected hindpaw and the number of foot withdrawals was counted. Stimulation of normal human skin with the weak (34.3 mN) and stronger (92.2 and 197.2 mN) VFHs elicits a sense of pressure and pricking pain, respectively. Therefore, a significant increase in the frequency of foot withdrawals in response to these mechanical stimuli was interpreted as mechanical allodynia (34.3 mN) and hyperalgesia (92.2 and 197.2 mN). Results are expressed as the mean ± standard error of the mean (S.E.M.). A Friedman test followed by Dunn's test were used for statistical analysis and differences were considered significant at the $P < 0.05$ level. All the experiments received approval from the Animal Care Committee of Nagoya University.

Withdrawal responses of experimental and control rats were examined for 3 weeks after the CFA and saline injections, respectively. In the control rats ($n = 8$), the saline-injected paw remained mostly unresponsive to the weaker VFH (34.3 mN) throughout the entire observation period (Fig. 1). Stronger VFHs (92.2 and 197.2 mN) induced a brisk but small and short withdrawal response in some control rats, and saline injection to the ankle joint did not cause any change in these responses. One week after the CFA injection, all experimental rats ($n = 8$) lifted the foot of the treated side more frequently in response to stronger

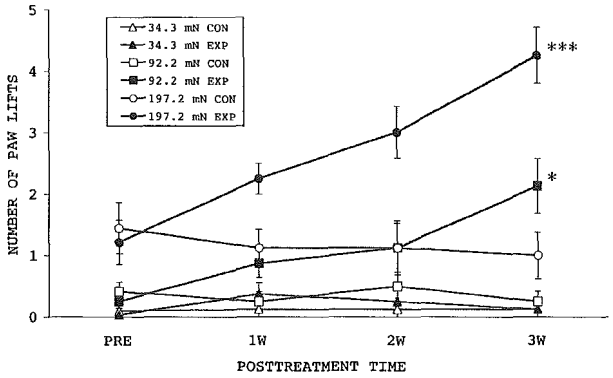


Fig. 1. The mechanical sensitivity of the hindpaw of the rheumatic (EXP) and control (CON) rats. The numbers of foot withdrawals to repeated mechanical stimuli with VFHs (34.3, 92.2 and 197.2 mN) are plotted against time. PRE, control period before treatment; W, weeks after CFA injection. Rats responded to stronger (92.2 and 197.2 mN) but not weak (34.3 mN) VFH to the hindpaw before the CFA treatment. After the CFA treatment, the numbers of paw lifts to the stronger VFHs started to increase gradually. Asterisks indicate values significantly different from the value obtained during the pretreatment control period (*$P < 0.05$, ***$P < 0.001$, Friedman test followed by Dunn's test).

VFHs (92.2 and 197.2 mN). Behaviors indicating pain such as licking or shaking the hindpaw often followed the paw lifting. At 3 weeks post-treatment, the numbers of paw lifts were significantly larger than the pretreatment control values (92.2 mN: $P < 0.05$; 197.2 mN: $P < 0.001$). Stimulations with a weak VFH (34.3 mN), on the other hand, seldom induced foot withdrawal in the experimental rats, and these were not influenced by the CFA treatment. These data imply that CFA-injection into the tibio-tarsal joint induced mechanical hyperalgesia but not allodynia in the adjacent plantar skin. Exposure experiments were therefore performed on a day when apparent hyperalgesia was observed during the post CFA treatment period between 20 and 27 days.

LP exposure did not affect the numbers of paw lifts in response to VFHs in the control rats (Fig. 2, for all VFHs: $P > 0.05$). In contrast to the controls, LP exposure in the CFA-injected rats, which were already hyperalgesic, clearly evoked a further increase in the numbers of paw lifts to stronger VFHs (92.2 and 197.2 mN) immediately after reaching the pre-set low pressure (MID I, $P < 0.05$ vs. PRE). Additionally, CFA-injected rats now showed an increased number of paw lifts to the weakest VFH (34.3 mN) used as well as allodynic behaviors such as licking or shaking the hindpaw (MID I, $P < 0.05$ vs. PRE). These increased hypersensitive behaviors quickly disappeared even though LP exposure was continued, and the number of paw lifts measured after 35 min of LP exposure (MID II, Fig. 2) had returned to the baseline levels. Return to the natural barometric pressure (POST) did not influence the responses to VFHs.

Fig. 3 shows the effects of LT exposure on mechanical hyperalgesia. The control rats showed no change in the numbers of paw lifts to the VFHs in response to LT (for all

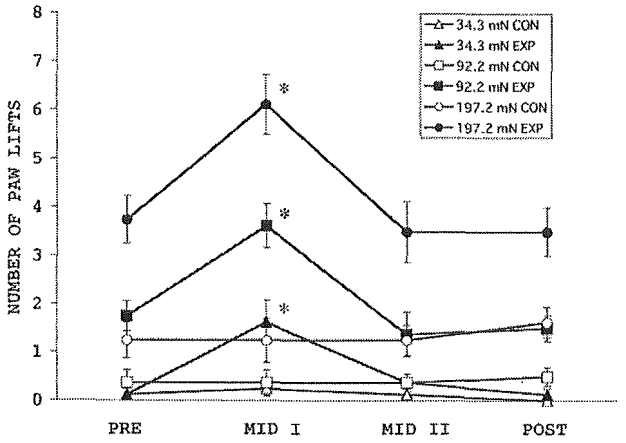


Fig. 2. LP exposure augmented mechanical hyperalgesia and developed mechanical allodynia in rheumatic rats. The numbers of foot withdrawals to repeated mechanical stimuli with VFHs (34.3, 92.2 and 197.2 mN) were plotted against measurements. CON, control rats; EXP, rheumatic rats. The period of measurement is expressed as PRE for the pre-exposure control period, MID I, II for the first and second measurements during LP exposure, respectively, and POST for the post-exposure period. See text for the precise timing of measurements. In the rheumatic rats, LP exposure increased number of foot withdrawals to strong (92.2 and 197.2 mN) and weak (34.3 mN) VFHs as well. Asterisks indicate values significantly different from the value obtained during the pre-exposure control period ($*P < 0.05$, Friedman test followed by Dunn's test).

VFHs: $P > 0.05$). In contrast CFA-treated rats clearly showed a further aggravation of mechanical hyperalgesia to LT exposure. Specifically, the numbers of paw lifts to the stronger VFHs (92.2 and 197.2 mN) gradually tended to increase, and 35 min after reaching the pre-set low temperature (MID II) the numbers were significantly larger than the baseline values (PRE vs. MID II; 92.2 mN: $P < 0.05$, 197.2 mN: $P < 0.01$). As in the LP environment,

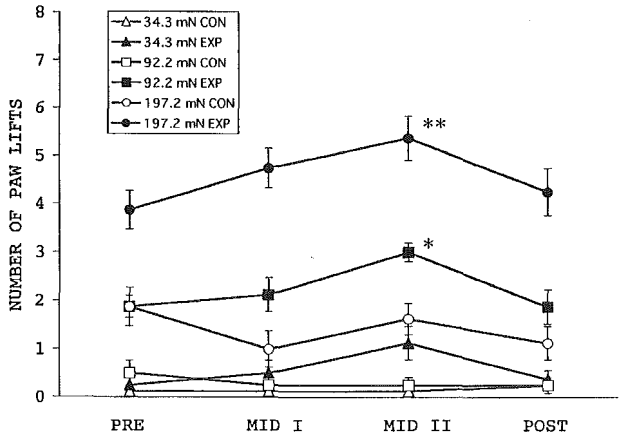


Fig. 3. LT exposure augmented mechanical hyperalgesia in rheumatic rats. The numbers of foot withdrawals to repeated mechanical stimuli with VFHs (34.3, 92.2 and 197.2 mN) were plotted against measurements. Presentation is similar to Fig. 2. In the rheumatic rats, LT exposure increased number of foot withdrawals to strong (92.2 and 197.2 mN) VFHs. Asterisks indicate values significantly different from the value obtained during the pre-exposure control period ($*P < 0.05$, $**P < 0.01$, Friedman test followed by Dunn's test).

some CFA-treated rats showed allodynic behaviors such as licking or shaking the hindpaw to the weaker VFH (34.3 mN) in the LT environment, although this was not a significant change. These signs of increased hypersensitivity disappeared 60 min after returning to the baseline temperature (POST).

The present experiment demonstrated that the numbers of paw lifts to the noxious mechanical stimuli (92.2 and 197.2 mN) were increased after CFA injection. This mechanical hyperalgesia was consistent with the previous observation [3]. The present data also demonstrated that LP and LT produced additional increases in the number of paw lifts to these noxious mechanical stimuli. Such meteorological changes led CFA-treated rats to further lift their paws to the innocuous mechanical stimulus (34.3 mN) as well. The augmenting effects of these exposures were not observed in the control rats. These results indicated that LP and LT not only aggravated the mechanical hyperalgesia but also induced the allodynia seen in animal models of rheumatic pain. These changes are similar to those observed in rats rendered neuropathic by CCI surgery to the sciatic nerve [11,12].

Noteworthy here is that LP augmented mechanical hyperalgesia and induced allodynia immediately after the lowest pressure was reached, and that these effects had disappeared at the second measurement 35 min later. This result agrees with our previous study with CCI rats, in which their increased mechanical allodynia in the hindpaw gradually disappeared with time in an LP environment [11]. These data therefore would suggest that this pain-aggravating process under pathological conditions is primarily activated by the onset of barometric pressure change rather than by absolute barometric pressure level.

Our previous observations that lumbar sympathectomy prevented the LP-induced augmentation of pain-related behaviors in CCI rats [11], and that LP transiently increased the blood pressure and heart rate of unrestrained normal and CCI rats [15] suggested that prompt activation of sympathetic nerves by an LP environment contributes to the LP effect on neuropathic pain. Although the influence of sympathectomy on the increased pain-related behaviors of arthritic rats in the LP environment was not tested, it is possible that LP-induced sympathetic activation also played an important role in the aggravation of arthritic pain in the present study. From this and our previous observation that LP environment did not decrease the hindpaw temperature of normal and CCI rats [11], we concluded that the mechanism of aggravation of neuropathic pain under an LP environment is not dependent on vasoconstriction. Rather, increased sympathetic nerve discharge may directly activate the cutaneous nociceptors and sensitize them to mechanical stimuli [2,13]. Since such novel adrenergic sensitivity of cutaneous nociceptors has also been found in CFA-induced inflammatory states [14], similar interactions may underlie the increased painful behaviors of arthritic rats in LP environments.

In contrast to the LP effect, a longer time of up to 35 min was required for the aggravation of pain under the LT condition in arthritic rats. We observed a similar time lag in the appearance of an LT effect on pain in CCI rats [12]. These data suggest that the pain-aggravating process activated by LT involves slowly progressing mechanism(s). Alternatively, this aggravation may be a result of gradual lowering of the skin temperature in the LT environment. A preliminary observation indicated that LT-exposure gradually decreased cutaneous hindpaw temperature of arthritic rats, and 10 ± 0.9 °C decrease was observed 35 min after reaching the pre-set temperature.

Recently, we have shown that LT exposure increased plasma norepinephrine level of normal rats [10]. This suggests, first, that LT exposure aggravates behavioral abnormalities of arthritic rats via an activation of the sympathetic nervous system, as in the LP effects described above. Second, there is another pain-aggravating process that acts through a mechanism that works only in arthritic rats, since augmentation of pain-related behaviors during LT exposure was found only in these rats. Our recent observations using single nerve recordings from the sural nerve of CFA-induced arthritic rats showed that the response to innocuous cold stimulation to the hindpaw skin was facilitated in C-fiber low-threshold mechanoreceptors (CLTM), and the proportion of cold sensitive C-fiber nociceptors was also increased [17]. In view of these results, one may expect that LT augments these cold-sensitive receptor activities in rheumatic rats, and this might be a mechanism for the LT-induced augmentation of guarding behavior (foot lifting without mechanical stimulation) seen in these rats (unpublished observation). Furthermore, the mechanical sensitivity of CLTM but not C-nociceptor units was increased in arthritic rats [17]. The data indicate that a CFA-induced inflammation induces sensitization of these receptors to mechanical stimulation as well. This supports the hypothesis that lowered local skin temperature during LT exposure increases sensitivity of these cutaneous receptors to noxious and innocuous mechanical stimuli to the hindpaw skin and then aggravates mechanical allodynia and hyperalgesia shown in rats rendered arthritic.

In conclusion, the present experiment demonstrated that simulated meteorological changes (LP or LT) augmented behavioral abnormalities in a model of rheumatic pain. These observations support reports from humans with chronic rheumatic pain indicating that pain is aggravated by an approaching low pressure system or exposure to a mildly cold environment [1,5].

References

[1] H. Aikman, The association between arthritis and the weather, Int. J. Biometeorol. 40 (1997) 192–199.

[2] D.F. Bossut, E.R. Perl, Effects of nerve injury on sympathetic excitation of A delta mechanical nociceptors, J. Neurophysiol. 73 (1995) 1721–1723.

[3] S.H. Butler, F. Godefroy, J.-M. Besson, J. Weil-Fugazza, A limited arthritic model for chronic pain studies in the rat, Pain 48 (1992) 73–81.

[4] A.M. Clarke, J. Nicholl, Does the weather affect the osteoarthritic patient? Br. J. Rheumatol. 30 (1991) 477.

[5] D. Guedj, A. Weinberger, Effect of weather conditions on rheumatic patients, Ann. Rheum. Dis. 49 (1990) 158–159.

[6] R.N. Jamison, Influence of weather on report of pain, IASP Newslett. Jul/Aug (1996) 3–5.

[7] W.R. Patberg, R.L.F. Nienhuis, F. Veringa, Relation between meteorological factors and pain in rheumatoid arthritis in a marine climate, J. Rheumatol. 12 (1985) 711–715.

[8] J.J. Rasker, H.J.G. Peters, K.L. Boon, Influence of weather on stiffness and force in patients with rheumatoid arthritis, Scand. J. Rheumatol. 15 (1986) 27–36.

[9] D.A. Redelmeier, A. Tversky, On the belief that arthritis pain is related to the weather, Proc. Natl. Acad. Sci. USA 93 (1996) 2895–2896.

[10] J. Sato, A. Ito, K. Mizumura, Lowering barometric pressure and ambient temperature increase the plasma norepinephrine release in unrestrained rats, Jpn. J. Physiol. 52 (Suppl.) (2002) S217.

[11] J. Sato, H. Morimae, Y. Seino, T. Kobayashi, N. Suzuki, K. Mizumura, Lowering barometric pressure aggravates mechanical allodynia and hyperalgesia in a rat model of neuropathic pain, Neurosci. Lett. 266 (1999) 21–24.

[12] J. Sato, H. Morimae, K. Takanari, Y. Seino, T. Okada, M. Watanabe, K. Mizumura, Effects of lowering ambient temperature on pain-related behaviors in a rat model of neuropathic pain, Exp. Brain Res. 133 (2000) 442–449.

[13] J. Sato, E.R. Perl, Adrenergic excitation of cutaneous pain receptors induced by peripheral nerve injury, Science 29 (1991) 1608–1610.

[14] J. Sato, S. Suzuki, T. Iseki, T. Kumazawa, Adrenergic excitation of cutaneous nociceptors in chronically inflamed rats, Neurosci. Lett. 164 (1993) 225–228.

[15] J. Sato, K. Takanari, S. Omura, K. Mizumura, Effects of lowering barometric pressure on guarding behavior, heart rate and blood pressure in a rat model of neuropathic pain, Neurosci. Lett. 299 (2001) 17–20.

[16] I. Strusberg, R.C. Mendelberg, H.A. Serra, A.M. Strusberg, Influence of weather conditions on rheumatic pain, J. Rheumatol. 29 (2002) 335–338.

[17] K. Takahashi, J. Sato, K. Mizumura, Responses of C-fiber low threshold mechanoreceptors and nociceptors to cold were facilitated in rats persistently inflamed and hypersensitive to cold, Neurosci. Res. 47 (2003) 409–419.

Japanese Acupncture and Moxibustion, JAM
Online English Journal of the Japan Society of Acupuncture and Moxibustion
10 May 2004 http://www.jsam.jp/

A proposal for a simple and useful research design for evaluating the efficacy of acupuncture: multiple, randomized n-of-1 trials

Kenji Kawakita K 1), Masao Suzuki 2), Kenji Namura 2) and Shouhachi Tanzawa 1)
1) Research Department of Japan Society of Acupuncture and Moxibustion
2) Department of Internal Medicine, Meiji University of Oriental Medicine

Abstract

[Aim] To develop an experimental design suitable for clinical acupuncture research.

[Design] Long-term n-of-1 trials (B-A-B-A design)

[Setting] University Hospital of Meiji University of Oriental Medicine

[Patient] A chronic bronchial asthma patient

[Intervention] Weekly acupuncture treatments for 10min with de-qi were given. The initial 10 treatments (period B1) were followed by 9 weeks baseline (A1), a second period of 12 treatments (B2.), and a further baseline period (A2).

[Main outcome measure] Asthma symptom score by diary

[Results] The patient's symptoms were clearly reduced during the treatment period but returned during the baseline period. These changes in asthma score were highly reproducible in this patient.

[Conclusion] The value of long-term n-of-1 trials in acupuncture research was clearly demonstrated, and it is suggested that the n-of-1 trial enables demonstration of the mi-byo-chi of acupuncture treatment. To increase the external validity of n-of-1 data, multiple, randomized n-of-1 trials is proposed as an appropriate design for clinical research into acupuncture.

Introduction

It is well recognized that the randomized controlled trial (RCT) is the most powerful experimental design for generating strong evidence (1). However, using the RCT to evaluate the clinical usefulness of acupuncture raises various issues that need to be resolved (2). One of the major problems is that the acupuncture treatment procedure is not fixed according to the disease or the patient's condition. Acupuncturists carefully select points for needle insertion that are individualized for each patient. This traditional approach to acupuncture treatment is very popular and has spread widely. The majority of acupuncturists who are clinically well trained reject the use of fixed points or a predetermined set of points when treating patients, as they believe that acupuncture with an incorrect choice

of points or inadequate procedures is ineffective. Their belief is usually based on clinical experience, not on evidence. They need to provide evidence to support their concept that the selection of points and other aspects of the process of acupuncture must be individualized in order to be effective. To evaluate the efficacy of acupuncture, various designs and types of control can be used, depending on the research question of the investigator (3).

N-of-1 trial as a useful design for acupuncture research

In the WHO guidelines on clinical research on acupuncture, single subject experimental designs (single case design, or n-of-1 trial) are introduced (4). N-of-1 trials (this term will be adopted in this paper) developed in the field of psychology, and have recently been adapted for clinical research (5-9). The statistical issues concerning the evaluation of the results have been clarified (10,11).

The simplest design of an n-of-1 trial is a reversal design. Baseline data are collected repeatedly during period "A" and their stability is confirmed, without treatment. Then a specific intervention is applied during period "B". The changes in outcome data are evaluated by visual inspection of a graphical figure or by the usual non-parametric test for two groups (12). Repeating the two stages of the trial (A-B-A-B-A-B- -) strengthens the plausibility of the results. The order BA instead of AB can be used when treatment is required urgently before the baseline period.

N-of-1 trials can evaluate the effectiveness of various specialized interventions in a number of patients who differ in several ways. They are easy to adopt for an exploratory study. The characteristics of the n-of-1 trial seem to be suitable for acupuncture research and the use of n-of-1 trials in acupuncture has been recommended (4, 13). However, the n-of-1 trial is not appropriate in cases where acupuncture treatments have long-lasting or irreversible effects. Moreover it has been pointed out that the results of n-of-1 trials cannot be easily generalized (14). Here we propose a unique protocol of n-of-1 trials that allows generalization from the results obtained from each patient attending an acupuncture clinic.

Long-term n-of-1 trials: a research design applied in an acupuncture clinic

In general, the majority of patients at acupuncture clinics seem to be regular attenders who visit the clinic each time their chronic illness deteriorates. Their complaints are treated successfully by acupuncture but will reappear after several weeks, months or years. Based on such a course of acupuncture treatment over time, we propose a new design for clinical research in acupuncture.

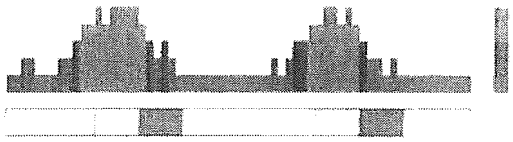


Figure 1: Hypothetical example of a long-term n-of-1 trial
A1, A2: baseline, B1, B2: intervention
Criteria for the onset of baseline data measurement should be determined in the protocol

Figure 1 shows a hypothetical illustration of a long-term n-of-1 trial (ABAB design). The upper figure shows the severity of symptoms and the lower bar shows the baseline (A1, 2) and

intervention (B1, 2) phases. In cases where patients' complaints are severe, the active intervention can be used first (BABA design). Another n-of-1 experimental design such as alternation may also be applicable. If the symptomatic changes produced by the intervention are very long lasting or permanent, a simple group comparison design should be used.

An example of a long-term n-of-1 trial in an asthma patient

The effects of acupuncture on chronic bronchial asthma were examined by n-of-1 trials (BABA design) in one patient. The patient, who was receiving care from a medical doctor but was resistant to steroid treatment (oral and by inhalation), was recruited to the study. The patient received acupuncture treatment (once a week, 10 times, repeated for a second course). Acupuncture needles (0.16mm in diameter, 40mm in length) were inserted and retained for 10 minutes at the following meridian points bilaterally: LI1, CV12, LI5, CV4, and B13. The severity of asthma was recorded by a dairy of asthma symptoms, a VAS of dyspnea, and Hugh-Jones classification. During the experiment the patient continued to receive steroids regularly.

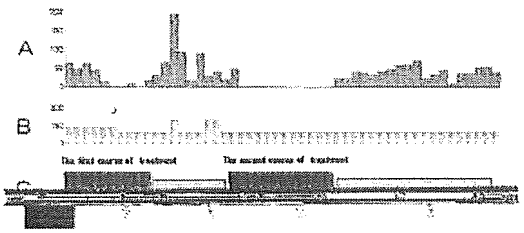


Figure 2: Example of a long-term n-of-1 trial of acupuncture for an asthma patient
A: score of the symptoms from asthma diary, B: dose of drug used, C: periods of treatment with acupuncture (B) and non-treatment baseline (A)

Figure 2 clearly shows that every symptom measure gradually improved, almost completely disappearing after the initial 10 weekly acupuncture treatments, and then rapidly returned to the pre-treatment level 9 weeks after cessation of treatment (initial BA session). The second treatment course of 12 weeks produced more rapid and sustained improvement during the treatment, but the symptoms again returned after treatment had stopped. Changes in the measures before and after the second treatment were as follows: Symptomatic scores: 66 to 0, VAS of dyspnea: 87 to 0, H-J classification: IV to I.

These results show that a long-term n-of-1 trial may be useful for demonstrating the effects of acupuncture on patients over a long treatment period. This kind of situation, with repeated treatments for chronic conditions, may be very common in acupuncture clinics. So, we propose a unique protocol to allow generalization from the results obtained from long-term n-of-1 trials.

N-of-1 RCT (randomized controlled trial)

The clinical usefulness of n-of-1 trial has become widely recognised, but, in respect of evidence based medicine (EBM) overall, its lack

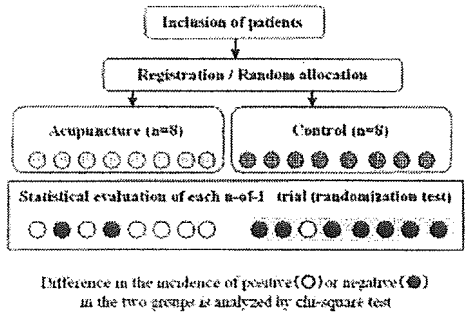


Figure 3. A block diagram of the protocol of multiple randomized n-of-1 trials

of external validity reduces the strength of evidence that it can contribute. In a recent EBM textbook, the n-of-1 RCT was ranked as the strongest evidence for making treatment decisions

(15). This high ranking of the n-of-1 RCT is mainly based on its high internal validity, that is, the n-of 1 RCT can make it possible to decide whether an intervention is suitable for a particular subject.

Patients are randomly allocated to each group then the effect of acupuncture or control intervention in each patient is evaluated by an n-of-1 trial (the randomization test can be used). Incidence of positive or negative results are analyzed statistically. (using chi-square test). In this case, chi square=6.3349 and p=0.0117. However, small samples require Yates' continuity correction, with which the results become, chi-square=4.063, p=0.0438. This result indicates the external validity of n-of-1 trials.

Table I:. A hierarchy of the strength of evidence for treatment decisions (Modified from ref #15)

1	N-of-1 RCT (randomized controlled trial)
2	SR of randomized trials
3	Single randomized trial
4	SR of observational studies addressing patient-important outcomes
5	Single observational study addressing patient-important outcomes
6	Physiologic studies (studies of blood pressure, cardiac output, exercise capacity, bone density, and so forth)
7	Unsystematic clinical observations

The simplest n-of-1 RCT is as follows: the patient is randomly allocated to two periods of interventions, either A/B or B/A. The efficacies of interventions A and B are evaluated by the use of appropriate outcome measures, and these alternating interventions continue until a significant difference is detected between their effects. If intervention A is superior to B, then A will selected as better treatment for the subject.
Regarding the analysis of n-of-1 data, various methodological issues have been identified. Time series analysis was strongly recommended instead of conventional group comparison tests (6,10). Other statistical tests such as C-statistics have also been proposed as an indicator for an n-of-1 trial (11). Recent developments in computer technology make it possible to use the randomization test to analyse the data from n-of-1 trials (16).

From the viewpoint of patient-oriented medicine, the n-of-1 RCT design is valuable and highly recommended. However, it should be noted that an n-of-1 RCT does not provide external validity. In Sackett's standard textbook of EMB, the n-of −1 RCT is not included in his classification of clinical trials and list of recommendations (Table II), but he noted the importance of the design and stated guidelines

Table II: Levels of evidence and grade of recommendations modified from ref #17)

Grade of recommendation	Level of evidence	Design of clinical trials
A	1a	SR (with homogeneity) of RCT
	1b	Individual RCT (with narrow confidence interval)
	1c	All or none
B	2a	SR (with homogeneity) of cohort studies
	2b	Individual cohort study (including low-quality RCT)
	2c	"Outcome" research
	3a	SR (with homogeneity) of case-control study
	3b	Individual case-control study
C	4	Case series (and poor-quality cohort and case control studies)
D	5	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"

for limitations on its application (17). Every researcher agrees that a systematic review of homogenous RCTs is the best EBM methodology for providing external validity.

We now propose a method to increase the external validity of n-of-1 trials by adding a randomization procedure in the group comparison.

Multiple, randomized n-of-1 trials

We propose that multiple, randomized n-of-1 trials are a suitable design for increasing the external validity of a single n-of-1 study. Figure 3 shows the outline of the protocol. Patients who match the entry criteria are registered and randomly allocated into the acupuncture and control groups. Their condition or symptoms are treated by various acupuncture techniques,

depending on the practitioner's method of diagnosis and treatment. the details of which should be reported in detail following the STRICTA recommendations (18). The effect on each patient is evaluated by a suitable statistical method such as a non-parametric test (12), then the incidence of positive and negative results is compared between the two groups using a chi-square test.

To conduct this protocol successfully, several issues should be considered. The symptom should be stable over a long period and responsive to the intervention. The severity of the major symptom or the overall condition should be recorded daily during the experimental period by simple questionnaire or VAS scale. When the symptom appears to be stable (an essential inclusion criterion). baseline data are collected (period A: days, weeks or months), then the intervention is applied repeatedly (period B: days, weeks or months). Follow-up data are also collected. The interventions should be repeated at least twice to increase the reliability of results. This protocol is easy to conduct if suitable patients can be recruited. If the sample size is large enough to allow a subgroup analysis, the effectiveness of various combinations of symptoms and methods of acupuncture treatment may also be examined by the incidence of positive of negative results.

The concept of "mi-byo-chi " for the acupuncture treatment

In general. the majority of patients at acupuncture clinics are regular and they feel that felt individual symptoms getting worse to maintain restore their a good health. If the treatment is performed when the symptom is not so too severe, the results will be better than those obtained those applied when the symptoms getting more severe. Figure 4 schematically illustrates the concept of "mi-byo-chi ".

The borderline between health and disease is not completely clear. In the ancient Chinese literature (the Yellow Emperor's textbook), the concept of mi-byo-chi was introduced. The "Mi-byo" means that the condition is pre-symptomatic, and "chi" means treatment, so the phrase indicates the importance of giving treatment before the symptoms become severe. When the treatment (thick black band) is applied to a condition that is less severe (B), the symptoms are abolished more rapidly than when it is applied to a condition that is more severe (A) (Fig. 4).

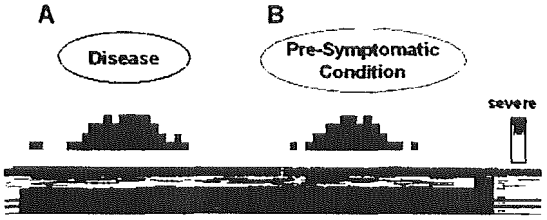


Figure 4: A schematic illustration of the concept of the "mi-byo-chi"

A: treatment of the developed disease takes a long time, B: treatment of the pre-symptomatic condition is rapidly effective.

This concept clearly highlights the importance of the preventive aspect of acupuncture treatment. For evaluating the validity of the concept of "mi-byo-chi", the proposed multiple randomized n-of-1 trial may be applicable and would be worth conducting in a large sample in order to increase both internal and external validity of the clinical trial and provide stronger evidence.

Acknowledgement

The authors wish to express their thanks to the late Dr. Kuwata for his valuable suggestions and discussions. This study was supported by the Foundation for Training and Licensure

Examination in Anma-Massage-Acupressure, Acupuncture And Moxibustion.

References

1) Sackett DL. Richardson WS. Rosenberg W and Haynes RB. Evidence based Medicine, 1st ed, Churchill Livingstone, 1998

2) White A, Filshie J, Cummings TM. Clinical trials of acupuncture: consensus recommendations for optimal treatment, sham controls and blinding. Comp Ther in Med 2001; 9: 237-245.

3) Sherman KJ, Lao LX. MacPherson H et al. Matching acupuncture clinical study designs to research questions. Clin Acupunct Orient Med 2001; 3: 12-15

4) WHO Regional Office for the Western Pacific, Guidelines for clinical research on acupuncture, WHO Regional Publications, Western Pacific Series No.15. 1995

5) Guyatt GH, Keller JL, Jaeschke R, Rosenbloom D, Adachi JD and Newhouse MT, The n-of-1 randomized controlled trial : Clinical usefulness, Ann Intern Med 1990;112: 293-299

6) Vincent CA. The treatment of tension headache by acupuncture: a controlled single case design with time series analysis. J Psychoson Res 1993; 34: 553-561.

7) Kawakita K, Okada K and Kuwata S. Application of n-of-1 trial and C statistics on Acupuncture Research, Proceeding of the workshop at WFAS in New York, 1996.

8) Guyatt G, Sackett D. Taylor DW, Chong J, Roberts R. and Pugsley S, Determining optimal therapy-randomized trials in individual patients, New Engl J Med 1986;314: 889-892.

9) Mahon J, Laupacis A. Donner A and Wood T, Randomized study of n-of-1 trials versus standard practice, B M J 1996; 312: 1069-1074.

10) Horne GP, Yang HCK and Ware WB, Time series analysis for single-subject designs, Psychol Bull 1982; 91: 178－189.

11) Kawai I, Kawamoto H and Oïkouchi H, Applications of C statistic to test the treatment-effects in single-subject designs, Jpn J Behav Analysis 1988; 2:36-47.

12) Edgington ES, Nonparametric tests for single-case experiments. In: TR Kratochwill and JR Levin (Eds), Single-Case Research Design and Analysis, Lawrence Erlbaum Associate. London, 1992. p133-157.

13) Kuwata S. Introduction of single subject designs as new experimental designs (II) Analytical evaluation of experimental data, Jpn. J. Acupunct Mox 1993; 43: 36- 43.

14) Kazdin AE, Single-Case Research Designs, New York, Oxford University Press. 1982, p368.
Guyatt GH and Drummond R. User's guided to the medical literature: Essentials of evidence-based clinical practice. Amer Medical Assoc Press. 2002.

15) Todman JB. Dugard P. Single-case and small-n experimental designs: A practical guide to randomization tests. Lawrence Erlbaum Assoc Inc. 2000.

16) Sackett DL. Straus SE. Richardson WS, Rosenberg W and Haynes RB, Evidence based Medicine. 2nd ed. Edinburgh. Churchill Livingstone, 2000

17) MacPherson H, White A. Cummings M et al. Standards for reporting interventions in controlled trials of acupuncture: the STRICTA recommendations, Comp Ther in Med. 2001; 9: 246-249.

Trigger point acupuncture treatment of chronic low back pain in elderly patients – a blinded RCT

Kazunori Itoh, Yasukazu Katsumi, Hiroshi Kitakoji

Kazunori Itoh
research assistant
licensed acupuncturist
Department of Clinical Acupuncture and Moxibustion

Yasukazu Katsumi
professor
Department of Orthopaedic Surgery

Hiroshi Kitakoji
professor
licensed acupuncturist

Meiji University of Oriental Medicine
Kyoto, Japan

Correspondence:
Kazunori Itoh

k_itoh@
muom.meiji-u.ac.jp

Abstract

Objective There is some evidence for the efficacy of acupuncture in chronic low back pain, but it remains unclear which acupuncture modes are most effective. Our objective was to evaluate the effects of two different modes of trigger point acupuncture on pain and quality of life in chronic low back pain patients compared to standard acupuncture treatment.

Methods Thirty five consecutive out-patients (25 women, 10 men; age range: 65–81 years) from the Department of Orthopaedic Surgery, Meiji University of Oriental Medicine, with non-radiating low back pain for at least six months and normal neurological examination, were randomised to one of three groups over 12 weeks. Each group received two phases of acupuncture treatment with an interval between them. Nine patients dropped out during the course of the study. The standard acupuncture group (n=9) received treatment at traditional acupuncture points for low back pain, while the other acupuncture groups received superficial (n=9) or deep (n=9) treatments on trigger points. Outcome measures were VAS pain intensity and Roland Morris Questionnaire.

Results After treatment, the group that received deep needling to trigger points reported less pain intensity and improved quality of life compared to the standard acupuncture group or the group that received superficial needling to trigger points, but the differences were not statistically significant. There was a significant reduction in pain intensity between the treatment and interval in the group that received deep needling to trigger points ($P<0.01$), but not in the standard acupuncture group or the group that received superficial needling to trigger points.

Conclusion These results suggest that deep needling to trigger points may be more effective in the treatment of low back pain in elderly patients than either standard acupuncture therapy, or superficial needling to trigger points.

Keywords

Trigger point, low back pain, elderly, randomised controlled trial.

Introduction

Chronic low back pain (LBP) is a major health problem in modern society. Seventy to eighty five percent of the population will experience back pain at some time in their lives.[1] Each year, 5–10% of the workforce is off work because of their LBP, but most of them are off for less than seven days. Almost 90% of all patients with acute LBP recover quite rapidly, regardless of therapy.[1] The remaining 10% are at risk of developing chronic pain and disability and account for more than 90% of the social costs for back incapacity.[2] The proportion of elderly patients who have LBP is greater than that of young adults.

In younger adults most back pain arises from the physical stresses on normal spinal structures,[3] whereas in the elderly, osteoarthrosis of the intervertebral joints and/or osteoporosis with collapse of the vertebral bodies is almost invariably present. Analgesia in the elderly is frequently unsatisfactory, and the incidence of adverse drug reactions, particularly to non-steroidal anti-inflammatory drugs (NSAIDs), is well known.[4] For this reason, many patients request physical therapies such as acupuncture.

Acupuncture has been frequently applied to chronic LBP. A number of randomised controlled trials on acupuncture for chronic LBP have already been published.[5,6] In 1997, during the NIH Consensus Conference, and more recently in

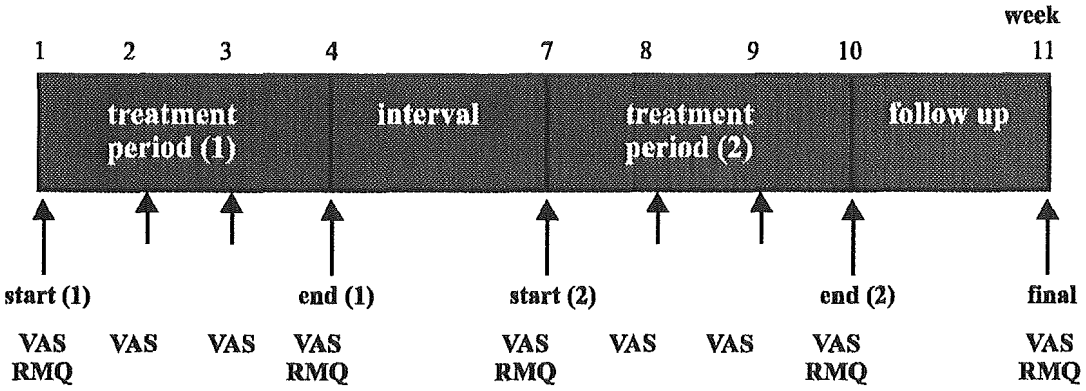


Figure 1 Time line of the trial. Evaluation was performed immediately before each treatment. VAS: visual analogue scale, RMQ: Roland Morris Questionnaire.

systematic reviews indicating equivocal results,[7] the question was asked: can acupuncture contribute to the conservative treatment of chronic LBP? The common conclusion was that all the studies conducted so far lacked adequate design and methodology, including adequate control of the quality of the administered acupuncture. Furthermore, the method of point selection in published trials seems to be more simple and formulary than that used in the standard acupuncture practice at our clinic. We believe that the response to acupuncture and therefore the success of a trial depends to an important degree on the choice and the number of points needled.

Our main aim in this study was to determine whether acupuncture at trigger points is an effective treatment for chronic LBP in the elderly, when compared to standard acupuncture at traditional points.

Methods

Patients

Patients aged 65 years or over with a history of LBP were recruited from the Meiji University of Oriental Medicine Hospital specifically for the study. Inclusion criteria were (1) lumbar or lumbosacral LBP for a duration of six months or longer; (2) no radiation of LBP; (3) normal neurological examination findings of lumbosacral nerve function, including deep tendon reflexes, plantar response, voluntary muscle action, straight leg raising, and sensory function; and (4) no previous treatment with acupuncture for LBP. Exclusion criteria were (1) major trauma or systemic disease; and (2) other conflicting or ongoing treatments. However, patients were included with medical conditions if there had been no change in drugs or dosage taken for one month or longer.

Patients who gave written informed consent were enrolled and randomly allocated, using a computerised randomisation programme, to one of three groups: the standard acupuncture (SA) group, who received acupuncture at traditional points for LBP, or the group that received superficial needling to trigger points (S-TrP) or the group that received deep needling to trigger points (D-TrP). Ethical approval for this study was given by the ethics committee of Meiji University of Oriental Medicine.

Design

The study was a subject and assessor blinded, randomised, controlled clinical trial. The three groups received two phases of acupuncture treatment with an interval between the two phases (the original design was a crossover study). Each phase lasted three weeks and the total experiment period was 12 weeks (Figure 1). Each patient received a total of six 30 minute treatments, one per week.

Blinding

Patients were blinded to their treatment. They were told before randomisation that they would be allocated to one of three treatments. The measurements were performed by an independent investigator who was not informed about the treatment allocation.

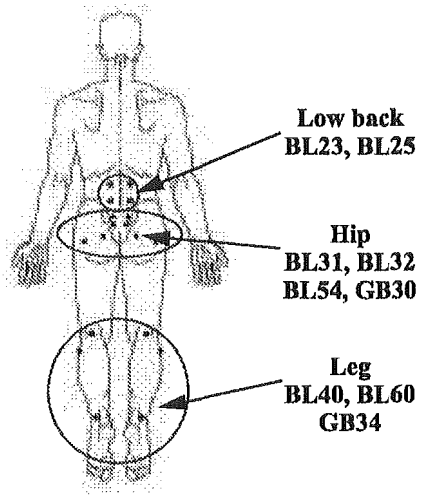


Figure 2 Acupuncture points used for treatment of the standard acupuncture group.

Treatment

The SA group received treatment at traditional points for LBP. After a literature review on acupuncture for LBP, only widely accepted acupoints were selected.[8–11] The standard points in the lumbar region (local points) were BL23, 25, and GB30; standard points on the lower extremity (distal points) were BL40, 60 and GB34. Additionally, up to four *ah shi* points of greatest tenderness were chosen, which were often close to, but not necessarily identical to, BL54, 31 and 32 (Figure 2). In the SA group, disposable stainless needles (0.2mm x 40mm, Seirin Co Ltd) were inserted into the muscle (to a depth of 20mm) and the 'sparrow pecking' technique (alternate pushing and pulling of the needle) was applied. When the subject felt dull pain or the acupuncture sensation *(de qi)*, the manipulation was stopped and the needle retained for ten more minutes.

The S-TrP and D-TrP groups received treatment at trigger points. The correct application of the technique requires experience in palpation and localisation of tender points in taut bands of skeletal muscle (myofascial trigger points). Precise needling of active myofascial trigger points provokes a brief contraction of muscle fibres. This local twitch response should be elicited for successful therapy, but it may be painful and post-treatment soreness is frequent.[12;13]

Table 1 **Muscles treated in the trigger point acupuncture group**

Muscle	S-TrP Group	D-TrP Group
Quadratus Lumborum	6	5
Iliopsoas	4	4
Piriformis	2	4
Gluteus Maximus	5	3
Iliocostalis Lumborum	1	3
Gluteus Minimus	0	1
Hamstring	1	0
Other	1	2

In this study, the most important muscles of the lumbar and lower extremity were examined for myofascial trigger points (Table 1). In the trigger point acupuncture treatment groups, disposable stainless needles (0.2mm x 50mm, Seirin) were inserted into the skin over the trigger point. In the S-TrP group, insertion was to a depth of about 3mm; in the D-TrP group the needle was advanced a further 20mm into the muscle. The 'sparrow pecking' technique was then applied. In S-TrP group, when the subject felt a kind of dull pain or acupuncture sensation *(de qi)*, the manipulation was stopped and the needle retained for ten more minutes. In contrast, in D-TrP group the manipulation was stopped when the local twitch response was elicited, and the needle retained for a further ten minutes. The mean number of insertions was 2.3.

The acupuncture was performed by an acupuncturist who had four years of acupuncture training and seven years of clinical experience.

Evaluation

Primary outcome measures were pain intensity, quantified using a 10cm visual analogue scale (VAS), and pain disability,[14] measured using the Roland Morris Questionnaire (RMQ).[15] The RMQ consists of 24 questions answered yes or no (range 0–24 points, the worst condition being 24).

The VAS measures were assessed immediately before the first treatment (pre) and one, two, three, six, seven, eight, nine, and twelve weeks after the first treatment. The RMQ measures were assessed before the first treatment and three, six, nine, and twelve weeks after the first treatment. The VAS and RMQ measures were completed by participants immediately before each treatment (Figure 1).

Table 2 **Characteristics of patients included in RCT of acupuncture**

Treatment Group	Trigger point acupuncture		Standard acupuncture
	Superficial needling	Deep needling	
Sample size	9	9	9
Age (y;mean±SD)	70.1±8.9	71.9±3.7	73.8±7.0
Diagnosis, number	Spondylosis 8 Osteoporosis 2 Compression fracture 1 Entrapment neuropathy 1	Spondylosis 8 Osteoporosis 3 Compression fracture 2 Entrapment neuropathy 2	Spondylosis 8 Osteoporosis 2 Compression fracture 1 Entrapment neuropathy 2
Pain duration (y;mean±SD)	5.2±2.6	7.4±4.5	5.4±3.7
VAS (mm;mean±SD)	65.6±17.1	65.6±17.3	64.0±20.2
Drugs treatment used for back pain	Poultice 7 Analgesic 3 Vitamin D 1 Bone resorption inhibitor 2	Poultice 6 Analgesic 3 Vitamin D 3 Bone resorption inhibitor 3	Poultice 5 Analgesic 2 Vitamin D 2 Bone resorption inhibitor 2

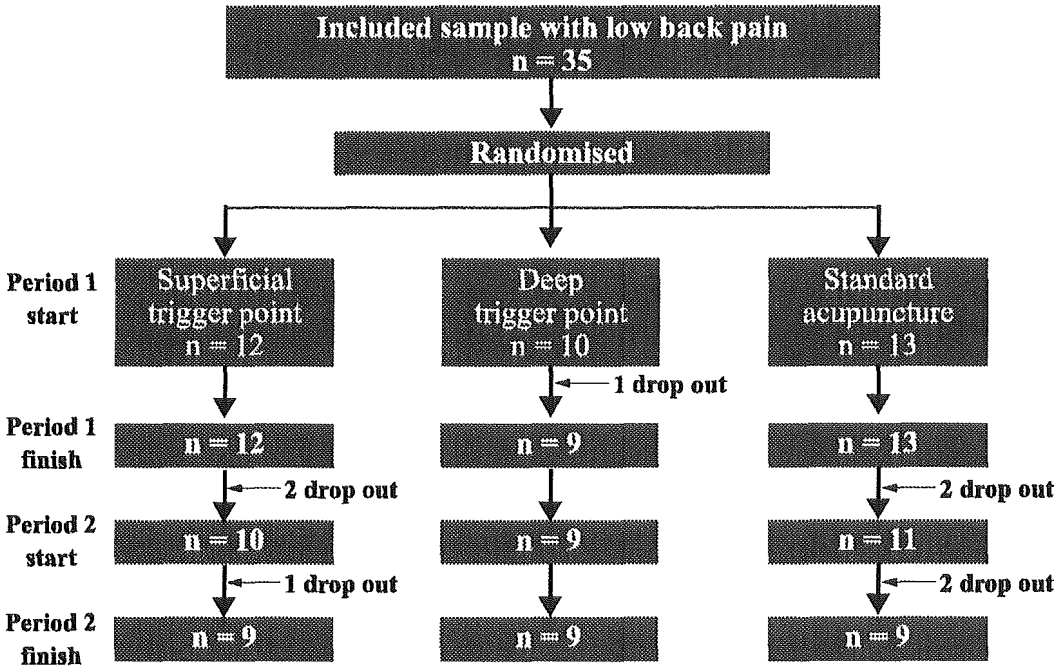


Figure 3 Participation flow in the study. Eight patients were excluded after dropping out.

Statistical analysis

The data are reported as means ± standard deviation (mean±SD). The nonparametric Tukey, Dunnett's multiple test, Fisher's exact test and one-way ANOVA (StatView v5; SAS Institute Inc, NC) were used for the statistical analysis. The level for statistical significance was set at $P<0.05$. Comparisons were made before and after each treatment, and between three kinds of intervention.

Results

Patient characteristics

Thirty-five patients (25 women, 10 men; age range: 65–81 years) were randomised and started treatment. No differences were found between the three groups regarding the variables measured at baseline including age, disease, pain duration, VAS and drug use (Table 2).

Patient progress through the trial is shown in Figure 3. Four patients in the SA group and three

Table 3 **Mean ± standard deviation of pain scores (VAS)**

Week	S-TrP Group	D-TrP Group	SA Group
1	65.6 ± 17.1	65.6 ± 17.3	64.0 ± 20.2
2	64.8 ± 17.5	50.8 ± 21.0	61.0 ± 23.1
3	50.1 ± 25.8	40.3 ± 21.0	55.0 ± 21.6
4	48.2 ± 30.5	33.1 ± 19.2	53.7 ± 21.9
7	52.7 ± 29.3	52.9 ± 22.5	56.8 ± 24.4
8	48.9 ± 30.8	41.8 ± 18.1	51.3 ± 25.1
9	53.9 ± 25.0	30.0 ± 13.4	46.4 ± 23.0
10	48.3 ± 27.9	23.1 ± 9.1	43.2 ± 23.1
13	50.1 ± 32.5	44.4 ± 19.1	56.8 ± 25.1

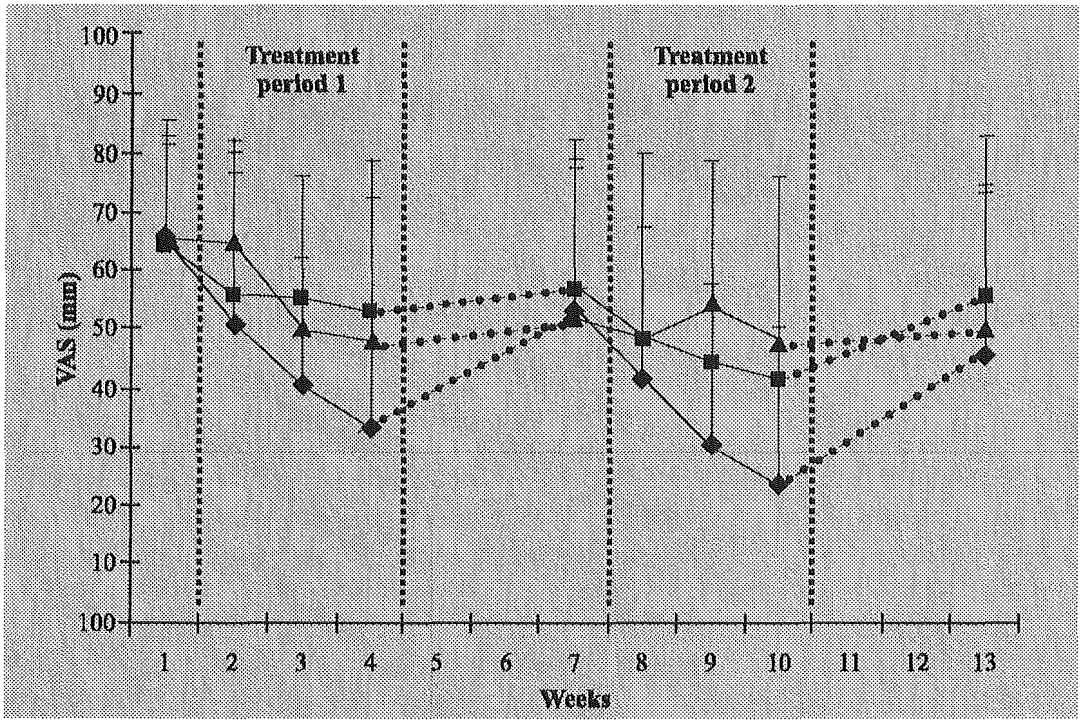


Figure 4 Effect of acupuncture on VAS score for chronic LBP. There were significant reductions in pain intensity between the treatment and interval for the deep trigger point acupuncture group (P<0.01, Dunnett's multiple test). By the end of treatment, the deep trigger point acupuncture group reported less pain than the other groups (difference not significant).
■: standard acupuncture group (n=9),▲: superficial trigger point acupuncture group (n=9),◆: deep trigger point acupuncture group (n=9).

patients in the S-TrP group dropped out as they had no response to treatment. Also, one patient in the D-TrP group dropped out due to adverse effects (deterioration of symptoms). The dropout rate was not statistically different between the groups (P=0.49, Fisher's exact test). The analyses were performed on the 27 patients who completed the study.

VAS score

As shown in Figure 4 and Table 3, the mean VAS scores tended to decrease from three weeks after the first treatment, although the time courses among the groups were different. In the D-TrP group, statistically significant differences were seen when comparing the VAS scores pre-treatment (66±17mm) with three weeks later

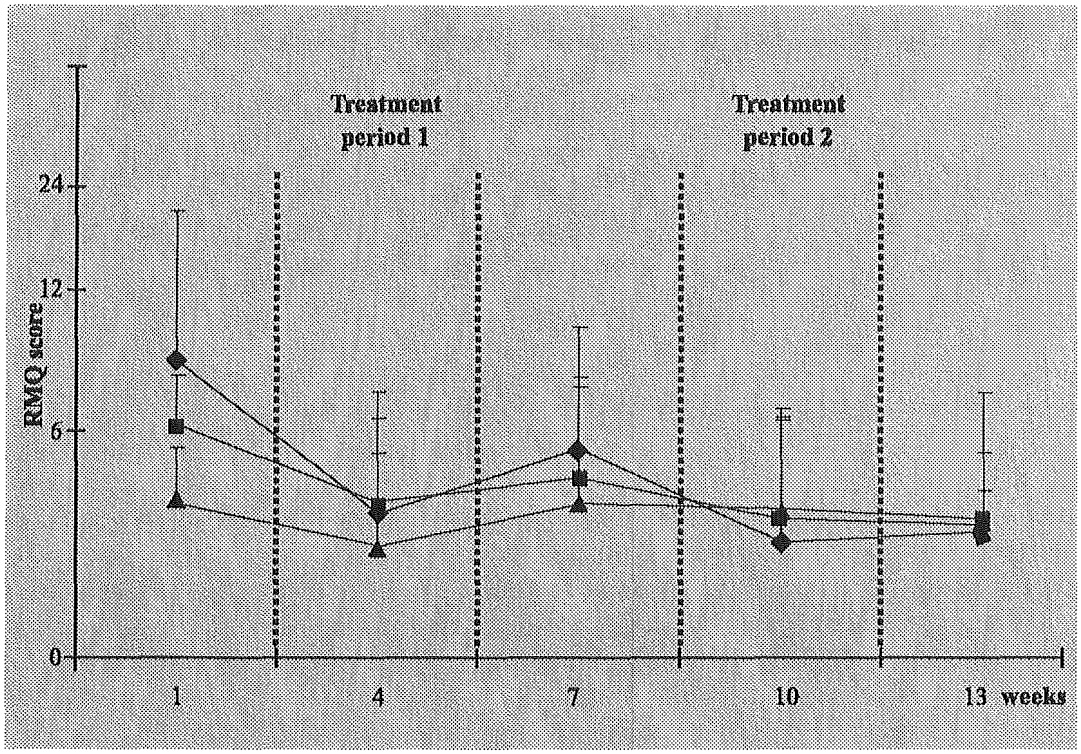


Figure 5 Effect of acupuncture on Roland Morris Questionnaire scores in chronic LBP. By the end of treatment, the deep trigger point acupuncture group showed the greatest improvement in scores, but the difference was not significant. The notation is the same as in Figure 3.

Table 4 **Mean ± SD Roland Morris Questionnaire scores**

Week	S-TrP Group	D-TrP Group	SA Group
1	5.0 ± 1.7	9.8 ± 1.9	7.5 ± 4.8
4	3.7 ± 2.8	4.8 ± 3.1	3.7 ± 2.8
7	5.1 ± 3.3	6.8 ± 3.8	5.9 ± 4.0
10	4.9 ± 3.6	3.8 ± 2.9	4.7 ± 3.7
13	4.3 ± 2.2	4.2 ± 1.2	4.2 ± 4.3

(33±19mm, P<0.01, Dunnett's multiple test). However, this improvement was reversed by the end of the interval (53±23mm). Significant improvements were again shown for VAS for the D-TrP group comparing pre-treatment and follow up (P<0.01, Dunnett's multiple test). There were no significant differences between pre-treatment scores and later scores for the SA or S-TrP groups.

By the end of the second treatment (nine weeks after the start of treatment), the D-TrP group reported relatively lower pain intensity than the SA or S-TrP groups, although the differences were not statistically significant (ANOVA).

Functional impairment

As shown in Figure 5 and Table 4, mean RMQ scores tended to decrease at three weeks after the first treatment, although the time courses were different between groups. In the D-TrP group, a statistically significant difference was observed comparing pre-treatment score (9.8±1.9) with three weeks later (4.8±3.1, P<0.01, Dunnett's multiple test), but there were no significant reductions in the scores for this period in the SA or S-TrP groups. By the end of the second course of treatment, the D-TrP group reported less pain intensity compared to the SA or S-TrP groups, but

the difference was not statistically significant (P>0.5, ANOVA).

Discussion

In the present study, there was a statistically significant reduction in both pain VAS and RMQ in the D-TrP group over the first treatment period, and for VAS over the whole time of treatment. There was no significant reduction in pain or RMQ for and SA or S-TrP groups. These results suggest that deep trigger point acupuncture therapy may be more effective than other forms of acupuncture therapy for LBP in elderly patients.

Chronic LBP is a very common complaint in elderly patients. Acupuncture treatment has been used for pain relief for a long time. Several studies have examined the efficacy of acupuncture treatment for chronic LBP.[16-19] As a consequence of the almost universal presence in the elderly of osteoarthrosis of the intervertebral joints and osteoporosis with collapse of the vertebral bodies, the muscles in the lumbar region and hip girdle are likely to have suffered stresses over a long period. Therefore, acupuncture treatment directed at the muscles has been advocated as an effective treatment of chronic LBP.

In a systematic review of acupuncture for LBP, Van Tulder et al included 11 clinical studies, eight of which compared acupuncture point stimulation with sham acupuncture.[6] No significant differences were found between the two stimulation techniques. In evaluating the efficacy of acupuncture, three important parameters are the site, mode and intensity of the stimulation. For assessing the parameter 'stimulation site', one can define the number of stimulation sites and their location (traditional acupoint or tender point/trigger point). In most previous studies, the stimulation sites were traditional acupuncture points.[16-19]

Our results suggest that the response to deep needling of trigger points may be greater than the response to needling the traditional acupoint, at least three weeks after the start of treatment. These results suggest that the stimulation site is important, and the acupuncture stimulation of myofascial trigger points might be most effective on chronic LBP in elderly patients.

The trigger point as a treatment site for acupuncture

The myofascial trigger point has been defined as a highly localised and hyper-irritable spot in a taut band of skeletal muscle fibres.[13] Important characteristics of a myofascial trigger point include tenderness, referred pain or referred tenderness, and a local twitch response.[20] Acupuncture or dry needling of a myofascial trigger point appears to provide immediate relief of pain related to that myofascial trigger point. However, the most effective form of acupuncture for treating myofascial trigger points is still unclear.

In this study, clinical results suggested that deep stimulation has a better analgesic effect than superficial stimulation, although the difference was not statistically significant. The strength of stimulation may depend on different parameters such as manipulating procedure, size of needle and the depth of needle insertion. It seems self-evident that there would be differences in the effects of superficial and deep insertion because of the different tissues that are stimulated. Deep insertion of the needle affects several structures (skin, fascia, muscle), whereas superficial insertion affects only the skin.[19;21] Myofascial trigger points are supposed to be sites where nociceptors, such as polymodal-type receptors, have been sensitised by various factors. In particular, sensitised nociceptors at the fascia might be possible candidates for the localised tenderness.[22] The polymodal-type receptors are also proposed as possible candidates for acupuncture and moxibustion because they respond to chemical, thermal, and mechanical stimulation, all of which can generate an analgesic effect.[23] These data suggest that acupuncture stimulation of myofascial trigger points in muscle may produce greater activation of sensitised polymodal-type receptors, resulting in stronger effects on pain relief. We should be aware of the fact that the polymodal receptors are distributed in the skin as well as the fascia and muscle, and should not exclude the possibility that superficial needling may activate polymodal receptors in the skin and produce analgesic effects.