

# Different patterns of blood flow response in the trapezius muscle following needle stimulation (acupuncture) between healthy subjects and patients with fibromyalgia and work-related trapezius myalgia

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## Abstract

Needle stimulation (acupuncture) has recently been shown to increase blood flow in the tibialis anterior muscle and overlying skin in healthy subjects (HS) and patients with fibromyalgia (FM). The aim of the present study was to examine the effect of needle stimulation on local blood flow in the trapezius muscle and overlying skin in HS and two groups of patients suffering from chronic pain in the trapezius muscle, i.e., FM and work-related trapezius myalgia (TM) patients. Two modes of needling, deep muscle stimulation (Deep) and subcutaneous needle insertion (SC), were performed at the upper part of the shoulder and blood flow was monitored for 60 min post-stimulation. Blood flow changes were measured non-invasively by using a new application of photoplethysmography. Increased blood flow in the trapezius muscle and overlying skin was found in all three groups following both Deep and SC. In HS, Deep was superior to SC in increasing skin and muscle blood flow, whereas in FM, SC was as effective as, or even more effective, than Deep. In the severely affected TM patients, no differences were found between the stimuli, and generally, a lesser blood flow response to the stimuli was found. At Deep, the muscle blood flow increase was significantly larger in HS, compared to the two patient groups. Positive correlations were found between muscle blood flow at Deep and pressure pain threshold in the trapezius muscle, neck movement and pain experienced at the stimulation, and negative correlations were found with spontaneous pain-related variables, symptom duration and age, pointing to less favorable results with worsening of symptoms, and to the importance of nociceptor activation in blood flow increase. It was hypothesized that the different patterns of muscle blood flow response to the needling may mirror a state of increased sympathetic activity and a generalized hypersensitivity in the patients. The intensity of stimulation should be taken into consideration when applying local needle stimulation (acupuncture) in order to increase the trapezius muscle blood flow in chronic pain conditions.

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## 1. Introduction

During recent years acupuncture has become a widely used treatment in Western countries to relieve pain in

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diverse acute and chronic pain conditions. Acupuncture comprises insertion of the needle into muscle tissue, mostly, followed by twirling the needle to elicit a distinct sensation of distension, soreness, heaviness or numbness (Cheng, 1987) and is suggested to relate to activation of thin A- $\delta$  and unmyelinated C-fibers (Andersson and Lundeberg, 1995).

Apart from pain-alleviating properties in certain pain conditions (Ernst and Pittler, 1998; Melchart et al., 2001) acupuncture has been shown to improve cutaneous microcirculation and tissue healing in musculoskeletal flaps in rats (Jansen et al., 1989a,b) and to increase circulation in the skin above the parotid glands (Blom et al., 1993). After acupuncture, improved salivation (Blom et al., 1992) and an increased level of the neuropeptide calcitonin gene-related peptide (CGRP) in the parotid glands have been found in patients with xerostomia (Dawidson et al., 1999). Following electro-acupuncture-like stimulation of the hindpaw in anaesthetized rats, increased muscle blood flow in the biceps femoris muscle was demonstrated using invasive laser Doppler flowmetry (LDF) (Noguchi et al., 1999). The mechanism underlying increased blood flow following sensory stimulation, such as acupuncture, has been suggested to rely on the activation of thin nerve fibers, which release vasoactive neuropeptides from their peripheral terminals upon activation, leading to vasodilatation and increased blood flow (Jänig and Lisney, 1989; Kashiba and Ueda, 1991; Sato et al., 2000).

One drawback of the invasive LDF technique in measuring muscle blood flow is the trauma caused by the insertion of the optic fiber into the muscle tissue, which per se may affect the blood flow. Photoplethysmography (PPG) is mostly used for skin blood flow monitoring (Challoner, 1979; Kamal et al., 1989). By using custom-designed optical probes with accompanying PPG instrumentation, PPG has recently been used for non-invasive measurements of muscle blood flow (Sandberg et al., 2004, 2003; Zhang et al., 2001). Following needle stimulation (acupuncture) increased blood flow in the anterior tibial muscle and overlying skin was shown in healthy subjects (HS) (Sandberg et al., 2003) and fibromyalgia (FM) patients (Sandberg et al., 2004). It was also shown that deep insertion into the muscle was superior to merely subcutaneous insertion of the needle in increasing blood flow. However, the subcutaneous needle insertion induced significantly larger increases in both skin and muscle blood flow in the FM patients than in the HS.

FM is a female predominant syndrome, characterized by widespread pain and tenderness and often accompanied by fatigue, sleep disturbances and psychological distress (Wolfe et al., 1990; Yunus et al., 1981). The pain in FM is commonly perceived as arising from muscles, and there are typically one or two locations that are the major pain foci, although sites of pain often shift

and fluctuate in intensity over days and weeks. A majority of FM patients report pain and stiffness in the neck-shoulder muscles, and a majority develop FM from localized or regional muscle pain conditions, such as trapezius myalgia (TM) (Henriksson and Sörensen, 2002). FM patients exhibit lower thresholds for mechanical pain (allodynia), and show exaggerated pain response to noxious stimuli (hyperalgesia) (Hurtig et al., 2001; Kosek et al., 1996; Lautenbacher et al., 1994). Although the anterior aspect of the tibia is not a spontaneously painful site in FM (Sörensen et al., 1998), a generalized hypersensitivity to pain exists, as well as additional abnormalities in the perception of somatosensory information (Kosek et al., 1996; Lautenbacher et al., 1994).

Various mitochondrial disturbances in type-I fibers and a reduced capillarisation per fiber cross-sectional area has been shown in patients with work-related TM (Kadi et al., 1998; Larsson et al., 2000, 2004). It has been suggested that such alterations are due to a reduced blood flow in rest and during exercise. Signs of microcirculatory disturbances are found in FM and it has been suggested that mitochondrial, microcirculatory and/or metabolic changes in the trapezius muscle might sensitize muscle nociceptors in these patients (Bengtsson, 2002).

The objective of the present study was to extend previous studies of non-invasive blood flow measurements in the anterior tibial muscle using noninvasive PPG, to the trapezius muscle. The aim was to investigate blood flow responses in skin and muscle to subcutaneous and deep needle stimulation in HS and in two groups of patients suffering from chronic pain in the trapezius muscle; i.e., FM patients and patients with work-related TM. Our studies of blood flow in the anterior tibial muscle and overlying skin showed a different pattern of blood flow response to subcutaneous needle stimulation between HS and FM patients. It was expected therefore that the two groups of patients had another pattern of blood flow changes in the trapezius muscle in response to needle stimulation than healthy controls.

## 2. Subjects and methods

### 2.1. Subjects

Twenty FM patients and seven unilateral, work-related TM patients were recruited from the Pain and Rehabilitation Centre at the University Hospital in Linköping, Sweden. The FM patients were diagnosed according to the ACR criteria of 1990 (Wolfe et al., 1990) by experienced physicians. The diagnosis requires two criteria, one of which includes a history of widespread pain for at least three months, including axial pain plus pain of both right and left sides of the body and above and below the waist. The second criteria includes pain in 11 or more out of 18 specified tender point

sites on digital palpation with an approximate force of 4 kilos. In order to recruit subjects with work-related TM the medical reports of former female out-patients due to neck myalgia and with no other diagnosis were identified and scrutinized. If it was confirmed that the myalgia had started in connection to assigned repetitive or static work tasks and continuously had worsened during working days the patients were asked to participate in the study. The patients were examined by means of a standardized clinical examination (Ohlsson et al., 1994) to ensure that the inclusion/exclusion criteria of work-related TM were met. The following inclusion criteria were used: pain should be present in the neck/shoulder region at the clinical examination, pain in the descending region of the trapezius muscle should be confirmed by a pain drawing, palpatory hard consistency of the trapezius muscle, normal strength, extensor reflexes and tactile sense of the upper extremities (according to standard clinical procedures) and both signs and symptoms should preferentially be found on the side regarded to be the side most exposed to occupational workload. Exclusion criteria were signs of tendinitis or joint affections in the shoulders, prior neck trauma or FM syndrome.

Nineteen healthy and pain-free females, age-matched to the FM group, were recruited from staff and students at the University hospital. Overall inclusion criteria for all subjects were female gender, Swedish-speaking, and aged between 20 and 60 years. Overall exclusion criteria were smoking, abuse of drugs or alcohol, neurological, psychiatric or cardiovascular disorders, any other severe disease, pregnancy or breast-feeding. Patient and subject characteristics are shown in Table 1.

All subjects were informed verbally and in writing about the experiments, and gave their informed written consent. The ethical principles in the Declaration of Hel-

sinki were followed, and the local Ethics Committee approved the study.

## 2.2. Assessment

### 2.2.1. Blood flow recording

PPG is originally a non-invasive optical technique for measuring peripheral blood circulation, e.g., in skin. The technique has also been utilized to record blood flow changes in the anterior tibial muscle (Zhang et al., 2001). In the present study a specially custom-designed 2-channel optical probe was developed and optimized for measurement of blood flow in the trapezius and supraspinatus muscle. The probe consisted of four photodetectors (PDs), four green (560 nm) Light Emitting Diodes (LEDs) and 2 near-infrared LEDs (804 nm) placed in a special pattern and embedded in black-colored silicon (Fig.1). The center-to-center distance between the LEDs and the PDs was 3.5 and 25 mm for the wavelengths 560 and 804 nm, respectively. The 560 nm LED monitors the superficial blood flow and the 804 nm LED the deeper blood flow, preferentially the muscle flow. The LED at 804 nm is to ensure that the blood flow signal will be insensitive to variations in oxygen saturation. A circular hole of diameter 7 mm was placed in the middle of the probe to allow the acupuncture needle to be inserted into the tissue. Another probe with only near-infrared LEDs was used for concomitantly measuring the trapezius muscle blood flow on contralateral side.

During evaluation of the probe an optical fiber was inserted into the trapezius muscle underneath the probe in 14 HS and connected to an optical power meter for recording and confirming that the light reached the muscle tissue. The location of the fiber tip was determined by ultrasound Doppler. The results showed in 14

Table 1  
Characteristics of healthy subjects (HS), fibromyalgia patients (FM) and patients with work-related trapezius myalgia (TM)

	HS (n = 19)			HS/FM <sup>a</sup>			FM (n = 19)			FM/TM <sup>a</sup>			TM (n = 6)			HS/TM <sup>a</sup>		
	Mean	SD	p	Mean	SD	p	Mean	SD	p	Mean	SD	p	Mean	SD	p			
Age (years)	36.3	6.8	ns	37.7	6.9	0.001	49.0	9.8	<0.001									
Symptoms (years)	0	0	ns	8.1	2.9	ns	7.8	5.5	NA									
Height (cm)	1.69	0.37	ns	1.67	0.73	ns	1.67	0.61	ns									
Body mass (kg)	65.5	7.2	0.002	72.0	11.2	0.001	64.3	7.4	ns									
BMI (kg/height <sup>2</sup> )	23.1	2.9	0.001	25.7	3.8	0.001	23.4	2.7	ns									
Spontaneous general pain (mm VAS) <sup>b</sup>	0	0	NA	46.1	21.9	ns	51.9	22.6	NA									
Spontaneous shoulder pain (mm VAS) <sup>b</sup>																		
Ipsilateral	0	0	NA	36.8	26.0	ns	40.0	19.4	NA									
Contralateral	0	0	NA	35.8	24.6	ns	38.9	27.0	NA									
Pressure pain threshold (kPa) <sup>b,c</sup>																		
Ipsilateral	184.5	64.5	<0.001	79.7	28.7	0.002	56.6	22.5	<0.001									
Contralateral	176.9	68.3	<0.001	83.0	30.3	0.011	63.6	27.3	<0.001									
AROM (degrees) <sup>d</sup>	57.1	6.0	<0.001	47.9	7.0	<0.001	38.7	5.0	<0.001									

<sup>a</sup> Mann-Whitney-U test was used to test differences between groups. NA = not applicable.

<sup>b</sup> Mean value from the three sessions.

<sup>c</sup> Max pressure was set to 325 kPa.

<sup>d</sup> (Flexion + extension + lateral flexion right + lateral flexion left + rotation right + rotation left)/6 in the neck.

subjects that the light penetrated down to a depth of 13.6 mm from the skin surface.

### 2.2.2. Distance to muscle fascia

The distance from skin surface to the fascia of the trapezius muscle was measured in 15 of the FM patients using ultrasound Doppler (Acuson 128XP/10).

### 2.2.3. Pressure pain threshold

An electronic algometer (Somedic®, Sweden) was used for pressure pain thresholds (PPT) on the upper part of the trapezius muscle bilaterally, as previously described (Persson et al., 2000). The site of the PPT measurement corresponds to acupuncture point GB 21 (Jenkins, 1990) and also to one of the tender points used for diagnosis in FM (Wolfe et al., 1990). The pressure was applied perpendicular to the skin at a speed of 30 kPa/s and the subjects were instructed to press a signal button when the pressure sensation changed to be perceived as a pain sensation. The maximum pressure was set to 325 kPa. The PPT measurements were conducted 3 times, and the mean of the last 2 measurements was calculated (Persson et al., 2000).

### 2.2.4. Range of movement

Active range of movement (AROM) in the neck was measured with the cervical range of motion instrument (CROM) (Hole and Bolton, 1995). The device consists of a plastic frame, mounted over the bridge of the nose and ears of the subject, and equipped with two gravity goniometers and a compass attached to the frame. Sitting on a stool the subjects performed maximum AROM in flexion, extension, and lateral bending and rotation of the right and left side. The sum of AROM was divided by six and used as an indicator of the total active range of movement in the neck.

### 2.2.5. Subjective ratings

The subjects estimated anxiety prior to the needling, and pain and discomfort experienced from the needle stimuli, using visual analogue scales (VAS) (McCormack et al., 1988). The scale consisted of a 0–100 mm horizontal line with the left endpoint depicting “not at all” and the right endpoint “worst imaginable”.

## 2.3. Intervention

The site of needle insertion was the highest part of the shoulder, corresponding to acupuncture point GB 21 (Jenkins, 1990) (Fig. 1). Two different modes of needling were performed in each patient; subcutaneous needle insertion (SC), and deep, ~10 mm insertion into the trapezius muscle (Deep). At SC, three needles of the dimension  $0.20 \times 15$  mm were inserted perpendicularly into the subcutis and left in situ for 20 min without further manipulation. At Deep, one needle of the dimension

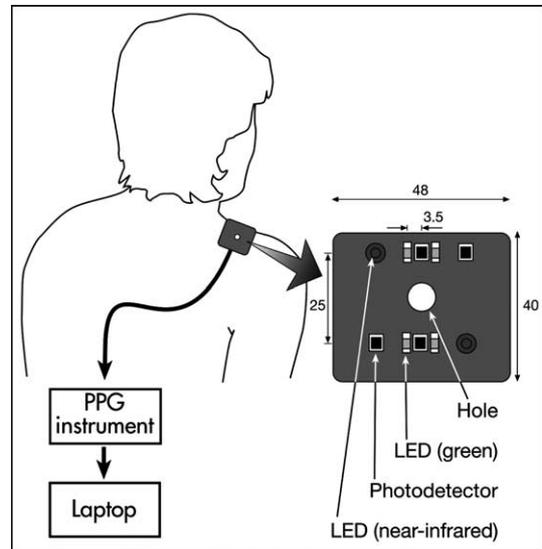


Fig. 1. The experimental set up including probe application site and instrumentation and details of the optical components and physical dimensions in mm.

$0.30 \times 30$  mm was inserted obliquely in the posterior direction and immediately followed by twirling the needle in order to elicit the specific sensation of distension, soreness, heaviness or numbness (Cheng, 1987). The twirling of the needle was repeated twice each 10th min, and after 20 min the needle was withdrawn. Sterile stainless-steel acupuncture needles were used (Hwato). One session, with no needling, served as control. The needle stimuli was performed by one of the authors (MS) with education in and clinical experience of Western acupuncture.

## 2.4. Procedure

Those subjects who had no previous experience of acupuncture had an initial individual visit to the department to experience the needling. All patients were instructed not to eat, to drink coffee, chocolate or tea, or to exercise within two hours before the sessions. The trials were conducted in a quiet room with moderate light and a temperature of 23–25 °C. Each patient participated in three randomly distributed sessions, separated by 2 days–2 weeks, each approximately at the same time of the day. The sessions included either of the two needle stimuli or a control situation with no stimulation.

After randomization, but before intervention, the subjects rated their anxiety about the intervention on VAS, and AROM and PPT measurements were performed. During the intervention, the patients sat in an armchair with their back supported up to the lower part of the scapulae and with their arms resting on a cushion on their knees. The subjects were instructed to sit as relaxed as possible and not move around. No talk was allowed during the blood flow recordings.

After ~20 min the probe was attached to the skin with adhesive tape on top of the shoulder and the LEDs were turned on. If necessary, the probe was moved slightly in order to get detectable signals. Blood flow was recorded for 60 s 10, 5 and 1 min prior to the intervention and continuously during the 20-min period of needle retention. After removal of the needle blood flow recordings were performed intermittently during 60 s every 5th min for another 40 min. At the control situation with no needle stimulation, an identical recording protocol was followed (Fig. 2). Immediately after the end of the trial, the patients rated pain intensity and discomfort experienced from the trial using VAS.

## 2.5. Statistics

The statistical packages Statview 5.1 (Abacus SAS Institute Inc., NC, USA) and SIMCA-P (version 10.0) were used for statistical analyses. In the figures, mean value  $\pm$  one standard error of the mean (SEM) is presented. The Friedman's two-way analysis of variance was used for comparing dependent variables, and if significant, Student-Newman-Keul's test was used. The Wilcoxon signed rank test was used for pairwise dependent comparisons and the Mann-Whitney-*U* test for independent comparisons.

All analyses were carried out using the area under curve (AUC) (blood flow vs. time) (Altman, 1999) for 4 periods as an outcome variable. The initial 5-min post-stimulation period is denoted T:1. The AUC for the following 15-min post-stimulation period (from 5 to 20 min) was divided by 3 in order to obtain a mean AUC for this period and is denoted T:2. The AUCs

including 20–40 and 40–60 min post-stimulation were divided by 4 in order to obtain mean AUCs and are denoted T:3 and T:4, respectively. Baseline, T:1, T:2, T:3 and T:4 are included in the analyses. Blood flow changes are expressed as mean percentages of the mean value obtained from the 60-s recording prior to the intervention (=baseline, denoted 0).

Principal component analysis (PCA) can be viewed as a multivariate correlation analysis. This analysis was performed in order to analyze the relationships between variables and to detect if a number of variables reflect a smaller number of underlying components using SIMCA-P (Eriksson et al., 1999). Principal components with Eigenvalues  $>2.00$  were considered as nontrivial components. A component consists of a vector of numerical values between  $-1$  and  $1$ , referred to as loadings. The loading expresses the degree of correlation between the item and the component. A loading is obtained for each measurement variable included in the PCA model. Variables that have high loadings (with a positive or negative sign) upon the same component are inter-correlated. We have considered loadings  $>0.25$  in absolute numbers (i.e., irrespective of sign) to be high and therefore of interest. Items with high loadings (ignoring the sign) are considered to be of large or moderate importance for the component under consideration. A cross-validation method, which keeps part of the data out from the model development to assess the predictive power of the model, was used to test the significance of the components. Outliers were identified using the two methods available in SIMCA-P; (1) score plots in combination with Hotelling's  $T^2$  (identifies strong outliers) and (2) distance to model in X-space (identifies moderate outliers).

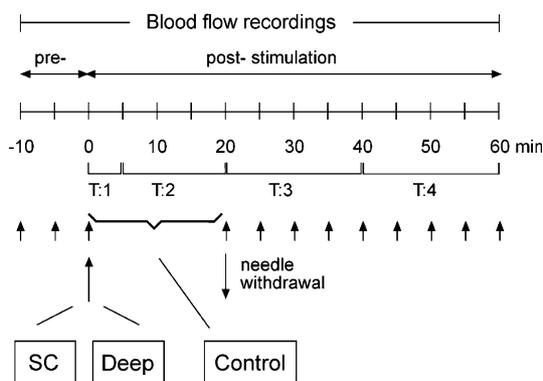


Fig. 2. Schematic protocol depicting the experimental design and procedure. The needle/s was inserted at 0 min and withdrawn at 20 min.  $\uparrow$  shows 60 s of blood flow recordings intermittently performed every 5th min.  $\frown$  shows 21 min of continuous blood flow recordings with the needle left in tissue, starting 60 s prior to intervention. Control period corresponds to the time of needles left in tissue. SC, subcutaneous needle stimulation; Deep, deep muscle stimulation, including manipulation of the needle three times; Control, rest only, without stimulation. T:1, T:2, T:3 and T:4 correspond to mean area under curve (AUC).

## 3. Results

### 3.1. Patient characteristics

Patient characteristics are shown in Table 1. All subjects fulfilled the three sessions of subcutaneous needle insertion (SC), deep needle stimulation (Deep) and the control session. Two patients were excluded from the analysis; signals from blood flow recordings of one FM patient were not possible to analyze and one TM patient was extremely stressed. Strong outliers in the FM group were identified and excluded; one at control skin blood flow, one at SC and Deep skin blood flow, and one at Deep skin blood flow. Since no differences existed between pain ratings, PPT or AROM values between the sessions within each group, means of the three sessions were used in the analyses and are presented in Table 1. Neither years of symptoms, nor pain ratings of local shoulder pain or general pain differed significantly between FM and TM. TM patients were

significantly older than the other two groups. Both patient groups had significantly lower PPT and AROM than the healthy group, and PPT and AROM values were significantly lower in TM than in FM. The distance between skin surface and muscle fascia was in mean (SD) 5.8 (1.7), range 3.4–9.7 mm, measured in 15 of the FM patients.

No complications or side effects caused by the interventions were observed or reported.

### 3.2. Blood flow changes at the different stimuli, including control

#### 3.2.1. Within-group changes

**3.2.1.1. Control.** Compared to baseline, skin blood flow was significantly increased at T:4 in FM. No significant skin blood flow changes were found in the other groups. Muscle blood flow was significantly increased at T:2 and T:3 in HS, at T:2, T:3 and T:4 in FM and TM, compared to baseline (Fig. 3(a)).

**3.2.1.2. Subcutaneous needle stimulation (SC).** When compared to control, SC resulted in significant skin blood flow increases at T:1, T:2 and T:3 in HS and FM, and at T:1 in TM. SC was significantly superior to control in increasing muscle blood flow at T:1, T:2

and T:3 in HS, at all time points in FM. In TM, muscle blood flow increased significantly only at T:1, compared to control (Table 2, Fig. 3(b)).

**3.2.1.3. Deep muscle stimulation (Deep).** Deep stimulation induced significantly larger skin blood flow changes than the control situation at T:1, T:2 and T:3 in HS, at T:1 and T:2 in FM and at T:1 in TM. Deep stimulation resulted in significantly larger muscle blood flow increase than control at T:1, T:2 and T:3 in HS and FM, with a tendency toward an increase also at T:4 in HS. In TM, muscle blood flow increased significantly more than control only at T:1 (Table 2, Fig. 3(c)).

**3.2.1.4. Deep vs. subcutaneous needle stimulation (SC).** In HS, Deep was superior to SC in increasing both skin and muscle blood flows at T:2 and T:3. In FM, in contrast, the SC mode of stimulation resulted in significantly larger increases in skin as well as muscle blood flow compared to Deep, appearing at T:1. No difference between Deep and SC on blood flow existed in TM (Table 2).

**3.2.1.5. Contralateral effects.** At control no differences were found between left and right trapezius muscle blood flow change in any group. At SC a transient

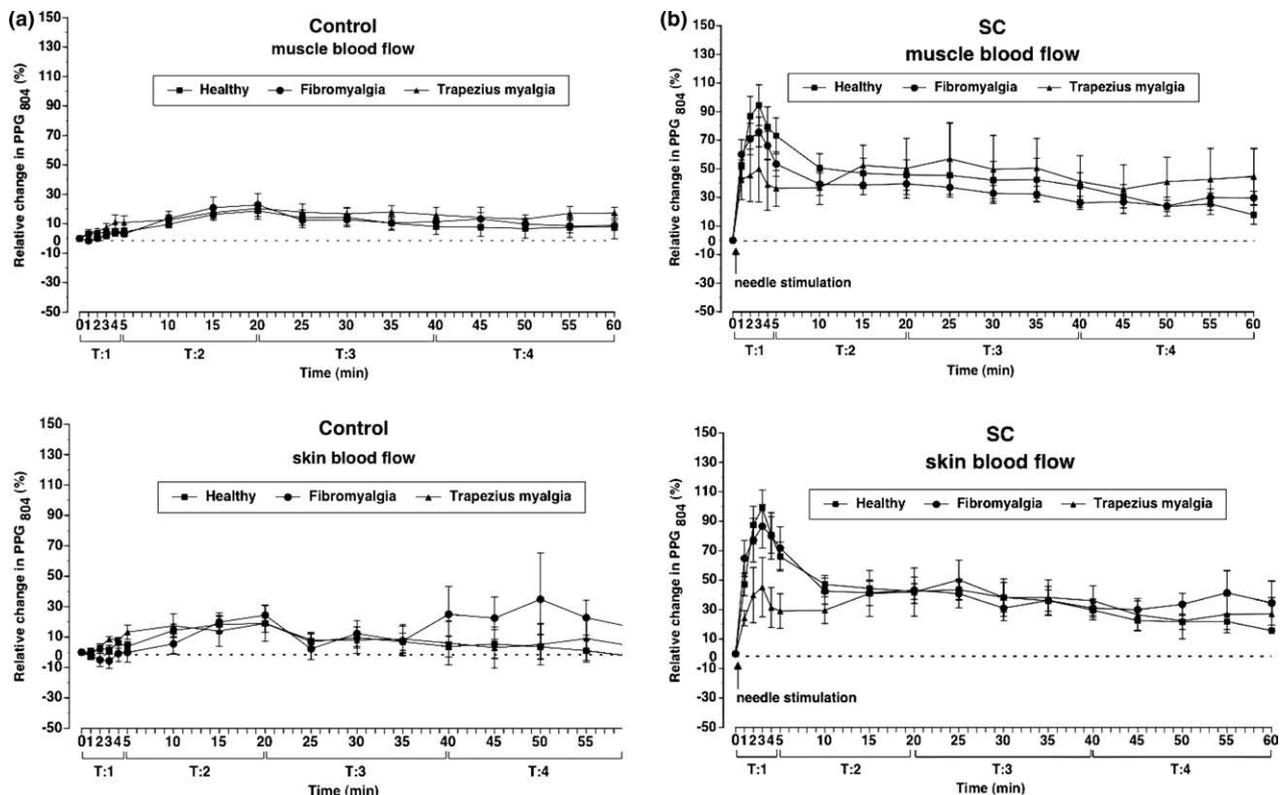


Fig. 3. Relative changes (%) in skin and muscle blood flow at: (a) control (no stimulation); (b) subcutaneous needle insertion (SC) and (c) deep muscle stimulation (Deep) in healthy subjects (HS), fibromyalgia patients (FM) and patients with trapezius myalgia (TM). The blood flow values are expressed as the mean ( $\pm 1$  SEM) 60 s prior to intervention, and corresponding time point for control. T:1, T:2, T:3 and T:4 correspond to mean AUC.

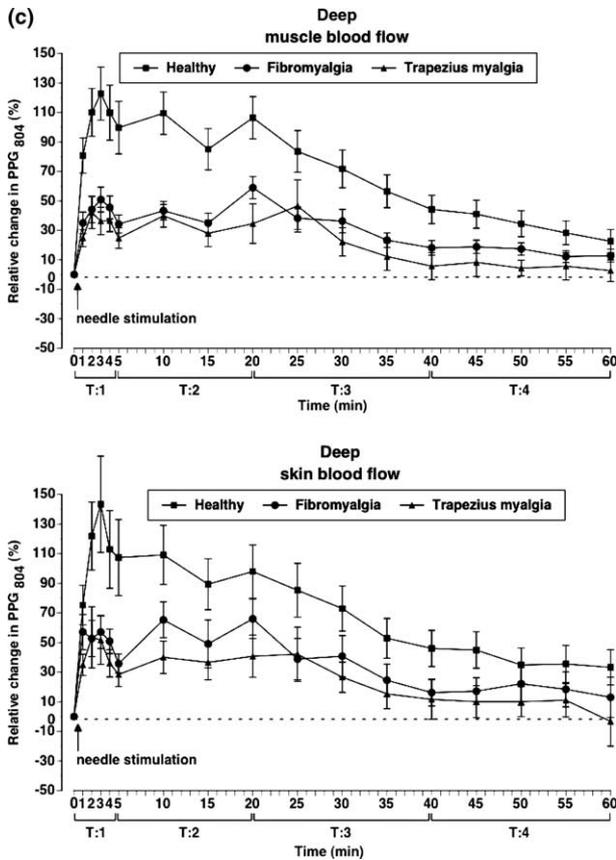


Fig. 3 (continued)

significant increase was found in both HS and patients. A transient significant increase was also found in HS at each of the three needle manipulations at Deep, in contrast to FM patients where contralateral blood flow increased transiently only at the first manipulation of the

needle. In TM patients no increase was found at Deep. Generally, the contralateral muscle blood flow increase was significantly less than in the stimulated muscle and apparent only at first minute after the needle stimulation in the patients and during 2 min in the HS.

**3.2.1.6. Between-group changes.** At control no significant differences in blood flow changes existed between the groups. At SC, a significantly larger skin blood flow was found at T:1 in HS, compared to TM. No differences existed in muscle blood flow changes between the groups at SC. Deep stimulation induced a significantly larger skin blood flow in HS than in FM at T:2 and a larger muscle blood flow increase at T:1, T:2 and T:3. Deep also induced a significantly larger skin blood flow increase in HS than in TM at T:2 and T:4, and a significantly larger muscle blood flow increase at all time points (Table 3).

**3.2.2. Psychological variables**

HS had significantly higher VAS ratings of anxiety, pain intensity and discomfort at Deep, compared to SC stimulation (Table 4). In FM and TM patients these ratings did not differ significantly between the two stimuli.

FM patients rated higher pain intensity at the SC stimulation than HS, but at Deep no difference in pain ratings existed between the groups. HS rated a higher degree of discomfort at Deep than the two patient groups.

**3.2.3. Results of multivariate analyses**

The relationship between a set of variables reflecting anthropometrical data, spontaneous pain and AROM (anthropometric variables, symptom duration,

Table 2

Statistical results of relative (a) skin and (b) muscle blood flow changes between subcutaneous needle insertion (SC), deep muscle stimulation (Deep) and control at different time points in healthy subjects (HS), fibromyalgia patients (FM) and patients with work-related trapezius myalgia (TM)

Time point	HS (N = 19)		FM (N = 19)		TM (N = 6)	
	p-value <sup>a</sup>	Post hoc-test <sup>b</sup>	p-value <sup>a</sup>	Post hoc-test <sup>b</sup>	p-value <sup>a</sup>	Post hoc-test <sup>b</sup>
<b>(a) Skin blood flow</b>						
T:1	<0.001	Deep, SC > control	<0.001	Deep, SC > control; SC > Deep	0.030	Deep, SC > control
T:2	<0.001	Deep, SC > control; Deep > SC	0.003	Deep, SC > control	0.513	NA
T:3	0.001	Deep, SC > control; Deep > SC	0.035	SC > control	0.311	NA
T:4	0.192	NA	0.607	NA	0.549	
<b>(b) Muscle blood flow</b>						
T:1	<0.001	Deep, SC > control	<0.001	Deep, SC > control SC > Deep	0.009	Deep, SC > control
T:2	<0.001	Deep, SC > control; Deep > SC	0.001	Deep, SC > control	0.311	NA
T:3	0.002	Deep, SC > control; Deep > SC	0.002	Deep, SC > control	0.607	NA
T:4	0.059	NA	0.002	SC > control	0.607	NA

T:1 denotes AUC for initial 5 min, T:2 denotes AUC for 5–20 min/3, T:3 denotes AUC for 20–40 min/4, and T:4 denotes AUC for remaining 40–60/4 min post-stimulation periods.

NA = not applicable. > = significantly larger than...

<sup>a</sup> Friedman's test was used to test differences between control, SC and Deep within each group.

<sup>b</sup> Student-Newman-Keuls test was used for post hoc tests.

Table 3

Statistical results of relative (a) skin and (b) muscle blood flow changes at control, subcutaneous needle insertion (SC) and deep muscle stimulation (Deep) between 19 healthy subjects (HS), 19 fibromyalgia patients (FM) and 6 patients with work-related trapezius myalgia (TM) at different time points

Time point	Control			SC			Deep		
	HS/FM <sup>a</sup>	HS/TM <sup>a</sup>	FM/TM <sup>a</sup>	HS/FM <sup>a</sup>	HS/TM <sup>a</sup>	FM/TM <sup>a</sup>	HS/FM <sup>a</sup>	HS/TM <sup>a</sup>	FM/TM <sup>a</sup>
<i>(a) Skin blood flow</i>									
T:1	NS	NS	NS	NS	0.031	NS	0.079	0.117	NS
T:2	NS	NS	NS	NS	NS	0.083	0.048	0.049	NS
T:3	NS	NS	NS	NS	NS	NS	0.080	0.096	NS
T:4	NS	0.025	NS						
<i>(b) Muscle blood flow</i>									
T:1	NS	NS	NS	NS	0.098	NS	0.003	0.011	NS
T:2	NS	NS	NS	NS	NS	NS	0.001	0.009	NS
T:3	NS	NS	NS	NS	NS	NS	0.027	0.039	NS
T:4	NS	0.046	NS						

T:1 denotes AUC for initial 5 min, T:2 denotes 5–20 min/3, T:3 denotes AUC for 20–40 min/4, and T:4 denotes AUC for remaining 40–60 min/4 poststimulation periods.

<sup>a</sup> Mann–Whitney-*U* test was used to test differences between groups.

Table 4

Visual analogue scale ratings (VAS in mm) of anxiety before, and ratings of pain intensity and discomfort following subcutaneous needle insertion (SC) and deep muscle stimulation (Deep) in 19 healthy subjects (HS), 19 fibromyalgia patients (FM) and 6 patients with work-related trapezius myalgia (TM)

	HS ( <i>N</i> = 19)			HS/FM <sup>a</sup>	FM ( <i>N</i> = 19)			FM/TM <sup>a</sup>	TM ( <i>N</i> = 6)			HS/TM <sup>a</sup>
	Mean	SD	Min–max		Mean	SD	Min–max		Mean	SD	Min–max	
<b>Anxiety</b>												
SC	2	5.6	0–21	NS	3	8.2	0–35	NS	0	0	0	NS
Deep	9	11.9	0–31	NS	7	15.3	0–51	NS	22	35.7	0–80	NS
Between stimuli <sup>b</sup>	0.017				NS				NS			
<b>Pain</b>												
SC	20	18.7	0–66	0.049	40	30.5	0–85.0	NS	21	24.3	0–64	NS
Deep	41	18.2	3.0–68	NS	45	26.4	4.0–88.0	NS	35	23.3	10.0–65	NS
Between stimuli <sup>b</sup>	0.004				NS				NS			
<b>Discomfort</b>												
SC	14	17.2	0–60	NS	15	20.3	0–57.0	NS	8	10.0	0–21	NS
Deep	31	21.2	0–70	0.011	16	21.0	0–70.0	NS	10	12.1	0–30	0.023
Between stimuli <sup>b</sup>	0.001				NS				NS			

<sup>a</sup> Mann–Whitney-*U* test was used to test differences between groups.

<sup>b</sup> Wilcoxon signed-ranks test was used to test differences between SC and Deep.

spontaneous pain intensity variables, PPT variables and AROM) and the three AUC variables (0–5 min, 5–20 min and 20–40 min) under the different conditions were investigated in different PCA:s in all subjects taken together. Only the AUC variables of muscle blood flow during deep muscle stimulation showed significant correlations with this set of variables ( $R^2$  cumulative = 0.53). The PCA identified two significant components. According to the first component (i.e., explaining most of the variance) the three AUC variables correlated positively and significantly with AROM, PPT and negatively (significantly) with the three spontaneous pain intensity variables and symptom duration (Fig. 4). The three AUC variables also loaded significantly upon the second component and correlated (positively) significantly with

pain intensity experienced at the stimuli, BMI, and body mass and negatively with age. In conclusion, the three AUC variables of muscle blood flow during deep stimulation both showed significant relationships with variables obtained prior to the tests and with a variable obtained during the stimulation.

#### 4. Discussion

The main findings from the present study were: (1) increased blood flow in the trapezius muscle and overlying skin following needle stimulation (acupuncture); (2) muscle blood flow change at the deep mode of stimulation correlated positively with PPT and AROM and negatively with pain variables, symptom duration and

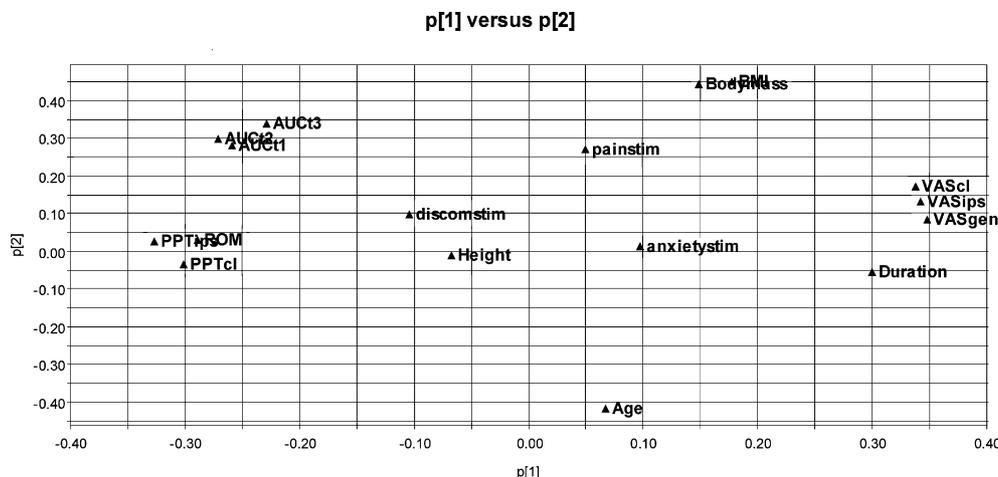


Fig. 4. The loadings of the two first principal components (first component  $p[1]$ : X-axis; second component  $p[2]$ : Y-axis) from a principal component analysis (PCA) of anthropometric variables (age, height, body mass, body massindex (BMI)), symptom duration (duration), pain intensity variables (pain intensity ipsilateral (VASips), pain intensity contralateral (VAScl) and pain intensity of generalised pain (VASgen), pressure pain threshold variables ipsilateral and contralateral (PPTips and PPTcl), three procedure variables (anxiety at stimulation (anxietystim), pain at stimulation (painstim) and discomfort at stimulation (discomstim)), range of motion (ROM) and the three AUC variables (0–5 min (AUCt1), 5–20 min (AUCt2) and 20–40 min (AUCt3)) in all subjects taken together ( $R^2$  cumulative = 0.53). Both components were significant (first component:  $R^2 = 0.39$ ; second component:  $R^2 = 0.15$ ).

age; (3) subcutaneously inserted needles, compared to deep muscle stimulation, were as effective as, or even more effective, in increasing blood flow in the trapezius muscle in FM, whereas the reverse was the case in HS.

#### 4.1. Methodological considerations

The technique of non-invasive measurement of deep blood flow, preferably from the tibialis anterior muscle, has been described earlier (Sandberg et al., 2004, 2003; Zhang et al., 2001). The Radiant Power of the near-infrared light has been shown to penetrate to a vascular depth of 13.0 mm from the skin surface overlying the tibialis anterior muscle (a submitted paper) and in the present study regarding the trapezius muscle the corresponding depth was 13.6 mm. Since the distance from skin to fascia was in mean (SD) 5.8 (1.7) mm, the near infra-red light was assured to penetrate into muscle tissue enabling muscle blood flow recordings. However, it must be pointed out that as for the tibialis anterior muscle the signal from the trapezius muscle to some extent contains flow information from the superficial vascular beds above the muscle. In the case of the tibialis anterior muscle this influence has been shown to be of importance when the blood flow increase in the skin exceeds approximately 100% (a submitted paper). In the case of the trapezius muscle, corresponding value is approximately 120% (unpublished material).

One drawback of the probe in previous studies (Sandberg et al., 2004, 2003) was a heating effect primarily from the green light source, leading to a local temperature increase and local blood flow regulation (a submitted paper). In the present study, the influence on blood

flow was reduced by at least 50% by shortening the pulse length of the pulsed light. Both skin and muscle blood flow at control in HS increased by  $\sim 15\%$  at T:2, with skin blood flow approaching baseline level again at 25 min. The increase in muscle blood flow was followed by a stepwise decrease, however not entirely back to baseline level. Since blood flow changes following needle stimuli consistently were compared to corresponding control values, this feature was assumed not to affect the results of the stimuli to a substantial degree.

In HS, no significant increase in either skin or muscle blood flow existed at the first 5-min period of control, indicating no temperature-induced influence on blood flow at this stage. This was the reason why the first AUC post-stimulation, i.e., T:1, included the first 5-min period. Remaining AUCs were calculated as mean AUC for 5 min in order to permit comparisons with T:1. AUC at T:4 (40–60 min) was excluded from the multivariate analysis since some patients changed their sitting positions at the end of the trial, possibly affecting blood flow.

#### 4.2. General considerations

Generally, the results in response to needle stimulation were in accordance with previous studies performed at the anterior aspect of the tibia (Sandberg et al., 2004, 2003) showing increased blood flow, as well as a different pattern of response in HS and FM, as was hypothesized. However, the studies are not completely comparable. In order to resemble a clinical situation of superficial acupuncture treatment in the present study, three needles (0.20  $\times$  15 mm) were inserted subcutaneously, in contrast

to one single needle (0.30 × 30 mm) in previous studies. Similarly, deep muscle stimulation in the present study involved needle stimulation (=twirling/rotation of the needle) repeated twice, in contrast to one single stimulation in the tibialis anterior muscle. Another important difference was the site of needle stimulation. The anterior aspect of the tibia is not a spontaneously painful site in FM, although embraced by a general hypersensitivity (Sörensen et al., 1998). In the present study the needling was performed at the most painful area of the body in the patients.

#### 4.3. Blood flow at control and in healthy subjects

In general, fairly large variations in blood flow existed among individuals at control. When muscle blood flow increased, the variability (for instance reflected in larger SE) of the AUC also increased. In general, skin blood flow varied less than muscle blood flow among individuals.

##### 4.3.1. Efferent function of sensory nerves

Upon activation, A- $\delta$  and C-fibers release vasoactive substances, such as CGRP and SP, antidromically from their peripheral nerve terminals by axon reflex mechanisms, known as part of neurogenic inflammation (Holzer, 1998; Maggi, 1991). CGRP is known as a very potent vasodilator, leading to increased blood flow (Jänig and Lisney, 1989; Kashiba and Ueda, 1991). Acupuncture is suggested to activate A- $\delta$  and C-fibers (Andersson and Lundeberg, 1995) and has been shown to increase skin blood flow in pain-free humans (Blom et al., 1993) and animals (Jansen et al., 1989a). In anaesthetized animals EA-like stimulation has been shown to increase muscle (Noguchi et al., 1999) and nerve (Hotta et al., 1996) blood flow. Evidence has been presented supporting the role of CGRP in the blood flow increase at noxious stimulation (Kashiba and Ueda, 1991; Loaliza et al., 2002; Sato et al., 2000). In the present study, three subcutaneously inserted needles induced increase in skin as well as muscle blood flow, however, the deep mode of stimulation was superior in increasing both skin and muscle blood flow in HS. The multivariate analysis revealed a positive correlation between pain experienced at the deep mode of needle stimulation and muscle blood flow increase, supporting the role of nociceptive input in vasodilatation and blood flow increase. This relation was apparent when needling the lower leg, too (Sandberg et al., 2003).

By antidromic activation of collaterals, nociceptive stimuli may also innervate adjacent tissue, resulting in vasodilatation and increases in blood flow extending the site of stimulation (Holzer, 1988). In addition, the existence of dichotomizing fibers of single sensory neurons innervating different tissues may explain blood flow modulation in skeletal muscle, secondary to stimulation

of the skin (Dawson et al., 1992; Sato et al., 1997). By activation of dorsal root reflexes, vasodilatation may appear bilaterally (Lin et al., 2000; Rees et al., 1996; Willis, 1999). Examples of subjects' drawings of body area getting warm following needle stimulation indicate the extent of these phenomena (Fig. 5).

##### 4.3.2. Sympathetic nerve activity

Except for the efferent function of thin sensory nerves in microcirculation, the role of sympathetic nerve activity should also be considered. Neuropeptide Y (NPY) is co-released with noradrenaline (NA) from sympathetic nerves and adrenal medulla during stress and exercise, causing vasoconstriction. Whereas NA-mediated vasoconstriction is quick in on- and off-set, NPY-mediated vasoconstriction is slow and of long duration (Zukowska and Lee, 2003). Normally, acute noxious stimulation, such as needling, increases the sympathetic tone and induces vasoconstriction (Sato et al., 1997). However, the immediately induced vasoconstriction due to the release of NA from sympathetic nerves, is normally overridden by locally released vasodilative substances from sensory nerve endings, resulting in vasodilatation (Häbler et al., 1997; Ochoa et al., 1993).

#### 4.4. Blood flow response in a chronic pain state

Subcutaneous needling is advocated by some authors, stating that the deep mode of stimulation involving twirling the needle will not be necessary, or will even be too forceful in treating some pain conditions, e.g., myofascial trigger points, with the risk of causing aggravated pain (Baldry, 2002). Superficial acupuncture was found superior to placebo in the treatment of low back pain (Macdonald et al., 1983) and in a variety of clinical trials on diverse pain conditions deep acupuncture has not been proven to induce significantly more pain relief than superficial acupuncture. Although unspecific effects are likely to contribute to these results, muscle blood flow increase due to the superficially inserted needles in the area of pain might improve the condition, and thus indirectly reduce pain. Based on the findings of enhanced muscle blood flow in the present study, superficial needling as reported by Baldry (2002) and Macdonald et al. (1983) may be considered appropriate in treating certain localized chronic pain conditions by its muscle blood flow enhancing effect.

##### 4.4.1. Fibromyalgia

In the present study, both modes of needle stimulation resulted in a blood flow increase in skin and muscle in FM, similarly to HS. However, one striking difference between HS and patients was the response pattern of blood flow following the deep mode of stimulation, being significantly less favorable in the patients than in HS. This finding was supported by the multivariate

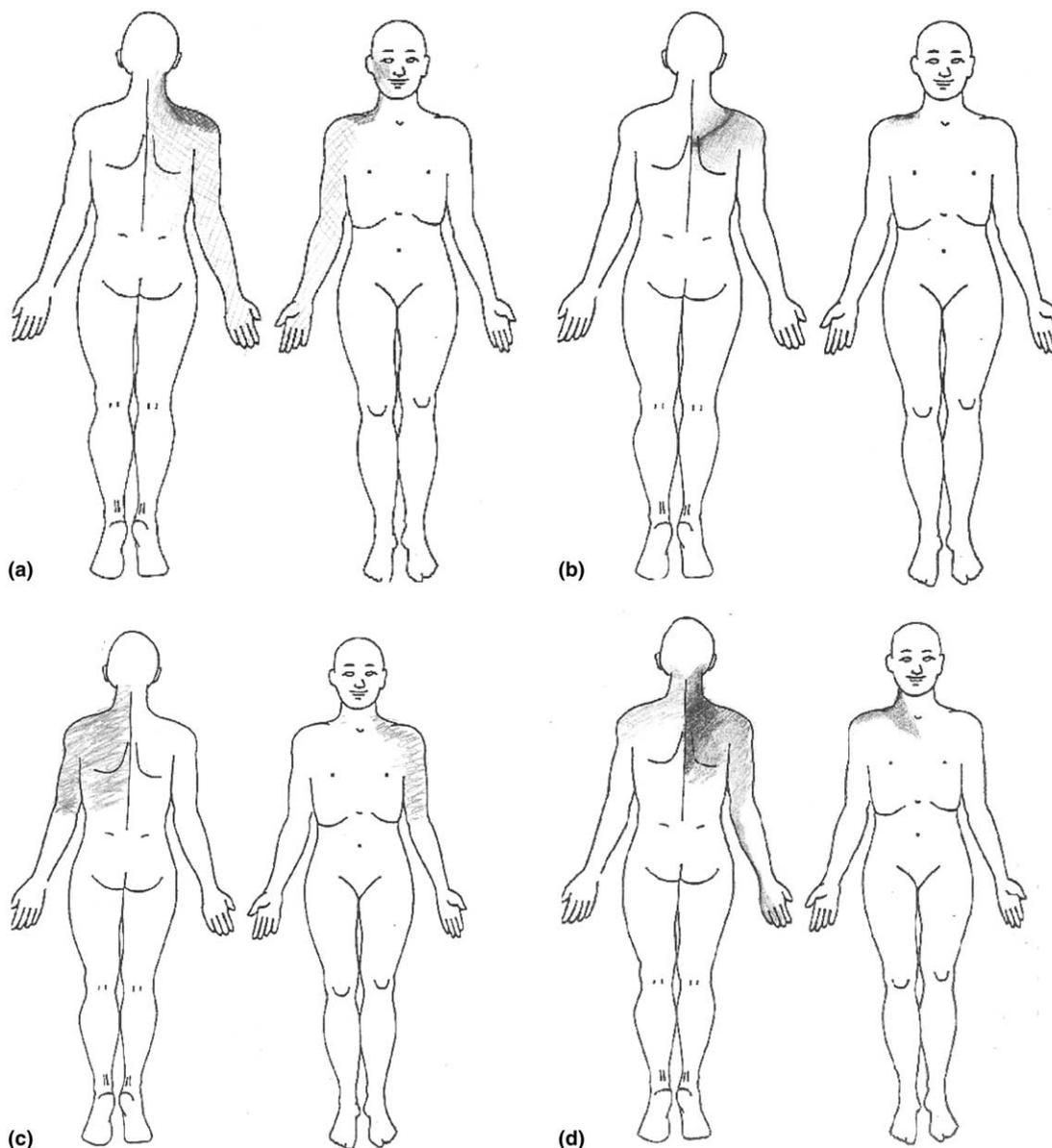


Fig. 5. Drawings illustrating the extension of warmth sensation experienced by two healthy subjects following (a) deep muscle stimulation (Deep) and (b) subcutaneous needle stimulation (SC), and by two fibromyalgia patients following (c) deep muscle stimulation (Deep) and (d) subcutaneous needle stimulation (SC). Notably, these drawings are not typical for any group, but chosen as examples of different patterns of warmth sensation following needle stimuli.

analysis on all subjects together, showing negative correlations between muscle blood flow at deep stimulation and pain variables (i.e., spontaneous pain intensity) and symptom duration, and positive correlations with AROM and PPT. In contrast, neither the significant blood flow increases nor pain ratings differed between HS and FM at deep stimulation into the spontaneously non-painful tibialis anterior muscle (Sandberg et al., 2004, 2003). In the present study, both HS and patients reported a pain intensity of approximately 40 on VAS at the deep stimulation into the trapezius muscle, pointing to nociceptor activation, yet the muscle blood flow increase was significantly less in the patients. These find-

ings indicate that in the spontaneously painful trapezius muscle of FM, the mechanisms behind muscle blood flow increase in response to intramuscular noxious stimulation are different compared to the non-painful tibialis anterior muscle, as well as compared to the trapezius muscle of HS. This indicates involvement of aberrant microcirculation in the trapezius muscle in FM, and possibly in TM.

Another apparent difference between HS and FM was the finding of subcutaneous needling being superior to the deep mode of stimulation in increasing both skin and muscle blood flow in FM. Of interest in this respect was that pain was rated equally intense at both modes of

stimulation in FM, while in HS the deep stimulation was perceived significantly more painful than the superficial. In addition, in FM the subcutaneous stimulation was rated significantly more painful than in HS. These findings indicate sensory disturbances in FM, influencing blood flow. Similarly, a significantly larger blood flow increase in FM than in HS was found in response to one needle insertion into subcutaneous tissue at the anterior aspect of the tibia, albeit very low pain ratings in both groups (Sandberg et al., 2004). These findings are supported by experiments on neurogenic flare responses to noxious mechanical stimulation, showing exaggerated flares in FM patients compared to HS (Gibson et al., 1994). A generalized, non-modality specific increase in pain sensitivity and additional abnormalities in the perception of somatosensory information has been shown in FM in various studies (Kosek et al., 1996; Lautenbacher et al., 1994), at least partly supporting the present and previous findings of different patterns of blood flow response to needle stimulation.

Both NPY and NA from sympathetic nerves inhibit the efferent function of free nerve endings in the periphery which will lead to vasoconstriction (Maggi, 1991; Zukowska and Lee, 2003). Especially when combined with hypoxia, NPY levels in plasma increase. Chronic pain may lead to plastic changes in the sympathetic nervous system (Roatta et al., 2003) and it has been suggested that patients with FM display a prominent dysautonomia, characterized as a sympathetic nervous system that is persistently hyperactive, but hypoactive to stress (Martinez-Lavin, 2002). Thus, under conditions of a high level of sympathetic activity, the release of vasoactive substances from free nerve endings in response to needle stimulation might be suppressed by increased sympathetic tone. The level of anxiety, as an indicator of mental stress before intervention, was equal in the three groups and was therefore not likely to explain the differences in blood flow response to the stimuli. It seems plausible that explanations to the aberrant pattern of the trapezius muscle blood flow in response to needle stimulation in FM may involve phenomena such as hyperactivity of the sympathetic nervous system, inhibiting release of vasodilative neuropeptides from sensory nerves, and hypersensitivity to somatosensory input.

#### 4.4.2. *Trapezius myalgia*

The TM patients presented with equal or even worse pain as revealed by VAS and PPT measurements, compared to FM. This means that not only the primarily affected shoulder but also the contralateral shoulder, as well as the body in general was affected by pain. This group responded less to the needling, with a blood flow increase only for the first 5 min. This may be due to various reasons, e.g., the relatively worse pain condition per se, obvious problems to remain sitting relaxed due to

aggravated pain, as well as being older. However, both the limited number and older age of the patients necessitate a cautious interpretation of the findings in this group. Altered processing of somatosensory input in these patients may be involved, similar to FM. Lowered PPTs bilaterally of the upper body (Madeleine et al., 1998) and a tendency to bilateral allodynia to pressure at perception threshold in the trapezius muscle have been shown in patients with work-related chronic neck-shoulder pain, as well as abnormal sensory perception in areas of referred pain (Leffler et al., 2003). In addition, biopsy studies have indicated various mitochondrial disturbances, indicating an ongoing energy crisis (Kadi et al., 1998; Larsson et al., 2000). Thus, the aggravated pain condition per se, involving alterations in the nervous system, and disturbances in the regulation of microcirculation might have contributed to the small changes in blood flow in response to needle stimuli in TM patients in the present study.

#### 4.4.3. *Contralateral effects*

The significant transient increase that was shown in contralateral trapezius muscle blood flow immediately with the stimuli may represent a sympathetic stress response. This would be in line with previously detected short-lasting increase in sympathetic nerve activity at each needle manipulation in HS (Sugiyama et al., 1995). Interestingly, this response also differed between HS and patients in that the increase in contralateral trapezius muscle blood flow was less prominent, or absent, in the patients.

## 5. Conclusion

One session of needle stimulation induced increased blood flow in the trapezius muscle and overlying skin in HS, and in FM and TM patients. Muscle blood flow change at the deep mode of stimulation correlated positively with PPT, neck movement, and pain exerted by the stimulation and negatively with spontaneous pain variables, symptom duration and age, pointing to less favorable results with the worsening of symptoms and older age, and to the importance of nociceptor activation in blood flow increase. In FM, subcutaneously inserted needles were as effective as, or even more effective, than deep muscle stimulation in increasing blood flow in the trapezius muscle, whereas the reverse was applicable in HS. Severely affected TM patients responded less to the stimulation. The intensity of stimulation should be taken into consideration when applying local needle stimulation in order to increase the trapezius muscle blood flow in chronic pain conditions, implying that subcutaneously inserted needles may be preferred to deep stimulation. The response of repeated sessions of needle stimulation (acupuncture)

on muscle blood flow is not known at present. The non-invasive technique of measuring deep blood flow is safe, simple and cheap, as well as being convenient to the patients. However, further adjustment of the probe will further improve the sensitivity.

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