Effects of electro–acupuncture on psychological distress in postmenopausal women

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SUMMARY. Objectives: To evaluate effects of electro–acupuncture (EA) on general psychological distress and relate to experience of climacteric symptoms in 30 postmenopausal women. Design: A randomised single-blind controlled design was used to evaluate effects of EA and extremely superficial needle insertion, with the latter serving as a near-placebo control. Settings: The Linköping University Hospital in Sweden. Interventions: Fourteen treatments during 12 weeks with follow-ups at 3 and 6 months. Outcome measures: General psychological well-being, mood and experience of climacteric symptoms. Results: Mood Scale improved only in EA group and not until 12 weeks compared to baseline, from 110 to 129 ($P = 0.01$), and to 120 at 3-month follow-up ($P = 0.04$). Mood was significantly better than control at 8 ($P = 0.05$) and 12 weeks ($P = 0.01$). Visual analogue scale estimation of climacteric symptoms was decreased at 4 weeks in both groups, and lasted throughout the study period, in EA group from 5 to 2 ($P = 0.04$) and in control group from 5 to 3 ($P = 0.02$) at 6-month follow-up. Well-being was ameliorated from 4 weeks in EA and from 8 weeks in control group until end of study ($P = 0.01$, $P = 0.03$). No significant differences on climacteric symptoms or well-being existed between the groups. Conclusions: This study does not show that EA is better than superficial needle insertion for the amelioration of general psychological distress and experience of climacteric symptoms in women with vasomotor symptoms after menopause. However, the more pronounced effect on mood suggests that EA might have additional effects compared with superficial needle insertion.

INTRODUCTION

Menopause

The majority of perimenopausal women suffer from vasomotor symptoms such as hot flushes and episodic sweating, which have a negative effect on the women's quality of life. Also, many women complain of tiredness and impaired working capacity, impaired mood states and other psychological symptoms.[1] The symptoms mostly occur during the first years postmenopause and subside after 4–5 years. However, in 10–15% of the women the symptoms persist more than 15 years.[2] A decrease in opioid activity[3] and an elevated sympathetic activity[4] have been proposed to be involved in the physiological mechanisms of hot flushes after menopause. Hormone replacement therapy is the treatment most prescribed, but alternatives are needed for women who are unable to use hormonal therapy for medical reasons or do not want to use hormones, because of unwanted side effects. One alternative might be

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acupuncture, which has been reported to induce beneficial effects on vasomotor symptoms in postmenopausal women.[5]

Acupuncture

Acupuncture was not widely introduced as an alternative in Western medicine until the scientific basis of acupuncture analgesia (AA) began to be explored in the middle of the 1970s. AA in man and animals is under most conditions reduced or abolished by the opiate antagonist naloxone, suggesting that a part of the effects may be attributed to endogenous opioids.[6] Over recent decades acupuncture has become a frequently employed treatment for chronic pain.[7–9] The magnitude of the increase in pain threshold, induced by acupuncture in chronic pain patients, is modified by psychological factors, and the pain relieving effect of acupuncture may be counteracted by the experience of stress or anxiety during stimulation.[10] Apart from pain inhibition, acupuncture also induces an increased sense of well-being, calmness and improved sleep in many patients, and in chronic pain patients, symptoms of depression and anxiety decrease after EA.[6,11] Antidepressive and sedative effects of EA may be attributed to increased synthesis and release of monoamines (serotonine, norepinephrine) and neuropeptides in the brain.[12–14] One neuropeptide, which has attracted much interest in this respect, is oxytocin.[15] In any medical circumstances, non-specific effects, or placebo responses, can be very powerful, and especially in acupuncture with its area of Eastern mysticism. The action of placebo is not limited to psychological responses but may also affect physiological processes.[16] The aim of the present randomised single-blind controlled trial was to evaluate the effects of EA on general psychological distress and relate to experience of climacteric symptoms in postmenopausal women. To achieve this, the effects of EA were compared with those of extremely superficially inserted needles (SNI), serving as a near-placebo control method.

MATERIALS AND METHODS

Subjects

Seventy-five women with postmenopausal vasomotor symptoms were recruited through advertisements in the local press and at gynaecological outpatient clinics. The women were asked to participate in a study evaluating different treatments for postmenopausal vasomotor symptoms: acupuncture ($n = 30$), oestrogen ($n = 15$), relaxation ($n = 15$) and physical exercise ($n = 15$). Before inclusion in the study the women underwent a general medical examination by a gynaecologist, and the postmenopausal status was verified by means of analysis of FSH and estradiol serum concentrations. Only women with a natural menopause of at least 6 months, aged between 48 and 60 years, were included in the study. Exclusion criteria comprised severe metabolic, thromboembolic, endocrine or malignant disease, uncontrolled hypertension (>95 mmHg diastolic blood pressure) or use of medication that could interfere with vasomotor symptoms. At the first visit to the gynaecologist, randomisation to any of the four treatments was performed by the use of identical, opaque, sealed envelopes, containing a label to determine the treatment. The 30 women randomised to acupuncture were again randomly allocated by sealed envelopes to EA or SNI at the first visit to the acupuncturist (MS). The randomisation was unknown to the gynaecologist and nurses evaluating the patients during the study. The present study will only account for the effects of acupuncture. All women were informed about the project, verbally and by written information, and gave their informed consent. The ethical principles in the Declaration of Helsinki were followed and the local Ethical Committee approved the study.

Treatments

Treatments were carried out at the Pain and Rehabilitation Centre at the University Hospital in Linköping by a physiotherapist (MS) with clinical experience of acupuncture in chronic pain and postmenopausal vasomotor symptoms.[5] Twelve sterile stainless-steel acupuncture needles were used at each session in both groups. In the EA group, the needles (Hwato, 0.30-mm diameter, 30-mm long) were inserted to a depth of 5–20 mm, depending on the location and the underlying structure, and twirled to evoke the DeQi sensation, characterised by a distinct sensation of distension, heaviness or numbness.[6,9] The DeQi sensation is suggested to relate to activation of A-delta-fibres from free nerve endings in the skin or from high-threshold ergoreceptors in muscle.[6] The acupuncture points used at each session were BL 15, 23 and 32 bilaterally (paraspinally at thoracic and lumbar levels), and SP 6 and 9 (lower leg), LR 3 (foot), HT 3, PC 6 (forearm) and GV 20 (head) unilaterally.[17] The choice of points was based on a previous study on vasomotor symptoms in postmenopausal women.[5] Thus, the acupuncture points were not specifically intended for psychological symptoms. After the DeQi sensation was achieved at all points, the four needles in the lower back were attached to an electrical stimulator (IC-1107, ITO CO., Ltd., Japan) giving low frequency alternating current stimulation (burst frequency of 2 Hz, with internal frequency of 80 Hz square wave pulses, pulse duration of 0.1 ms) with an intensity strong enough to elicit non-painful muscle contractions around the needles. No further DeQi sensation was sought for, after the current was applied. The current was usually increased once or twice during the stimulation period in order to maintain muscle contraction. In the SNI group, the

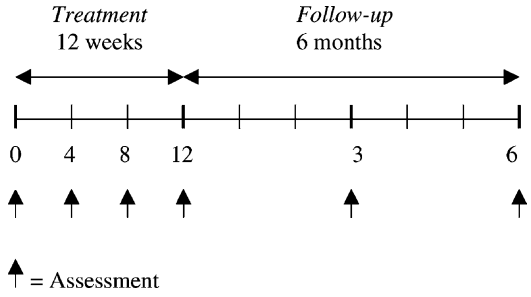

Fig. 1 Time schedule depicting treatment, follow-up periods and assessments (arrows) in the EA and SNI groups.

12 needles (Hwato, 0.25-mm diameter, 15-mm long) were attached to the skin extremely superficially, and 1–15 cm away from the acupuncture points used in the EA group. They were left hanging loosely down the skin, without any further stimulation. Only the small dimension needles were used, all of which were out of sight of the woman.

Each treatment session for EA as well as SNI lasted 30 min and was given twice a week during the two first weeks, and thereafter once a week for another 10 weeks. Thus, all women received 14 treatments over 12 weeks (Fig. 1). All women were comfortably lying in a lateral position, alone in a quiet room with a blanket, and pillows supporting the head and upper arm and leg. The therapist entered the room two to three times during the session to adjust the current intensity if needed, and otherwise to ensure that the woman was comfortable. During the sessions many of the women were half-asleep.

Assessments

Before start of treatment, after 4, 8 and 12 weeks of treatment, and at follow-up 3 and 6 months after completed treatment, the women filled in self-report scales at their visits to the Department of Obstetrics and Gynaecology (Fig. 1). Neither the nurse, responsible for the administration of the questionnaires, nor the gynaecologist was aware of the result of the randomisation. The primary measure in the present study was psychological distress, including mood, general psychological well-being and experience of climacteric symptoms.

Mood

The self-administered MOOD Scale was used. It is developed from earlier 'mood adjective checklists' and consists of six dimensions, of which three (pleasantness, activation and calmness) are considered to measure the bipolar dimensions of mood.[18] Data from these dimensions were used for the analyses, and are presented as a total sum score (MOOD Scale) with a min–max score 38–152, higher values indicating a better mood.

General psychological well-being

The Symptom Check List -90 (SCL-90) is a self-report clinical rating scale designed for use in symptomatic behaviour of psychiatric outpatients.[19] Five of the nine dimensions, measuring a domain of psychological well-being, were selected for the present study (somatisation, depression, anxiety, hostility and interpersonal sensitivity). Thus, the scale was reduced from 90 to 50 items and presented as a total sum score (SCL-50), with lower values indicating a better general psychological well-being.

General climacteric symptoms

The women estimated their experience of general climacteric symptom intensity (GCSI) using a visual analogue scale (VAS) with the left endpoint indicating 'no symptoms' and the right endpoint 'unbearable symptoms'. The use of VAS as a method of assessing climacteric symptoms is not validated, but used in a previous study.[5] The women's estimate comprised the entire climacteric symptomatology experienced.

Table 1 Social and medical characteristics of postmenopausal women who completed 12 weeks of treatment in the EA and SNI groups

		EA group ($n = 15$)	SNI group ($n = 13$)
Age	Years, mean (S.D.)	54.4 (3.6)	53.6 (3.0)
Duration of menopause	Years, mean (S.D.)	3.5 (2.3)	5.9 (4.4)
Weight	Kilograms, mean (S.D.)	70.8 (11.2)	71.2 (.8)
Height	Centimetres, mean (S.D.)	163.5 (6.9)	165.7 (5.0)
Body mass index[a]	Mean (S.D.)	26.7 (3.1)	25.6 (4.4)
Marital status	Married/cohabiting	14	12
	Single	1	1
Employee	Yes	14	13
	No	1	0
Education level	Compulsory school	9	6
	High school	4	5
	University degree	2	2
Smoking	Yes	3	4
	No	12	9
Exercise habits	Regular fitness exercise ≥ once/w	5	2
	Regular walking or cycling to work	2	1

[a] Weight/height^2 (kg/m^2).

Statistical analyses

In tables median values with interquartile ranges are presented. Wilcoxon Matched-Pairs Signed Ranks Test was applied for the pair-wise comparisons within groups, compared to baseline values. Mann–Whitney *U*-test was used for between-group comparisons. A *P*-value of <0.05 (two-tailed) was considered significant. A per protocol analysis was used to test the efficacy of the interventions. The sample size was based on results from an earlier, similarly designed study, in which EA showed a non-significant tendency toward better results compared to the control group.[5]

RESULTS

Social and medical characteristics of the study sample are shown in Table 1. On inspection, the baseline differences between groups were not marked. Fifteen women were randomised to the EA group and 15 to the SNI group. Before start of treatment, 1 of the 15 women randomised to SNI withdrew from the study because of troublesome migraine. Yet another woman in the SNI group was excluded from the analysis because of repeated non-attendance. Thus, 28 women, 15 in EA group and 13 in SNI group fulfilled all treatment sessions and completed the questionnaires during the treatment period of 12 weeks. At 3-month follow-up, three women were missing, two belonging to the EA and one to the SNI group. At 6-month follow-up another two women were lost from the EA group. Altogether, 23 women completed all follow-ups up to 6 months after end of the treatment period, 11 women in the EA, and 12 in the SNI group. The reason for withdrawal was in all cases initiation of hormone replacement therapy.

Short-term results—during the 12 weeks treatment period

MOOD Scale scores improved only in the EA group and not until 12 weeks compared to baseline. SCL-50 scores showed significant improvement up to 12 weeks in EA group, and at 8 and 12 weeks in the SNI group. Significant changes in GCSI were found within both groups during all treatment period. Improvements in the EA group were significantly more pronounced than in the SNI group on the MOOD Scale scores at 8 and 12 weeks. No other between-group differences existed. Within- and between-group results for the treatment period are presented in Table 2 and Fig. 2.

Long-term results—6 months follow-up

In the EA group, a significant change existed at 3-month follow-up on the MOOD Scale compared to baseline, whereas no change was found in the SNI group. Compared to baseline, the SCL-50 score was significantly improved at both 3- and 6-month follow-ups in both groups, as well as VAS estimations of general climacteric symptoms (GCSI). No significant between-group differences were found during the long-term follow-up. Long-term results are presented in Table 3 and Fig. 2.

DISCUSSION

Major findings

The results of the present study show that both EA and SNI were associated with increased well-being and reduced experience of climacteric symptoms. No significant differences between the EA and SNI groups were seen, except for mood, which was improved in EA group. The better results in the EA group on mood indicate that EA might have additional effects compared with SNI. Taken together, the results suggest that the needling situation itself causes strong unspecific effects, or placebo responses.

SNI as a control

The EA and SNI groups were managed identically, the only difference being strength of afferent sensory stimulation applied. The SNI technique used in the present study is not identical with 'superficial acupuncture' (SF), where needles are inserted into subcutaneous tissue to a depth of 3–10 mm. SF exerts less pain inhibitory effects than both deep manual acupuncture, eliciting the needle sensation of DeQi[9] and EA,[20] but cannot be considered a true placebo, since it still exerts somatic sensory stimulation from receptors in the skin, though minimal compared to EA. However, by functional magnetic resonance imaging (MRI), the DeQi sensation is shown to activate the hypothalamus and deactivate multiple limbic areas, as opposed to SF, where no effect on these systems could be registered.[21] 'Minimal acupuncture', with needles inserted 1–2 mm and stimulated extremely lightly, is described as a 'true'/'acceptable'/'near-placebo' control,[22] and resembles the SNI technique used in the present study. However, no stimulation at all was applied to the needles in the present study. They were out of sight of the women, and some of the extremely superficially inserted needles fell off immediately, or during the treatment session. Thus, special efforts were made to minimise the physiological response of the needles while maintaining its psychological impact in order to establish a near-placebo control.

Specific effects evoked by EA

In the EA group the DeQi sensation was elicited, followed by low frequency electrical stimulation, mainly activating A-delta-fibres from high-threshold

Table 2 Results (median values with interquartile ranges, Q1–Q3) from subjective ratings of mood (MOOD Scale), psychological well-being (SCL-50) and GCSI in postmenopausal women during 12 weeks of EA ($n = 15$) and SNI ($n = 13$)

Timepoint	Variables (min–max)					
	MOOD Scale (38–152)		SCL-50 (0–200)		GCSI (VAS 1–10)	
	EA MD (Q1–Q3)	SNI MD (Q1–Q3)	EA MD (Q1–Q3)	SNI MD (Q1–Q3)	EA MD (Q1–Q3)	SNI MD (Q1–Q3)
Baseline	110 (99.8–123.8)	118 (104.0–138.0)	41 (27.5–53.3)	37 (22.8–67.8)	5 (5.0–8.0)	5 (5.0–7.0)
4 weeks	113 (94.0–118.8)	109 (105.0–126.5)	26 (14.4–49.8)	31 (16.3–61.3)	4 (2.3–4.8)	4 (2.0–5.5)
P-value	0.73	0.16	0.02	0.09	0.02	0.02
8 weeks	120 (98.0–135.8) *	116 (103.0–125.3)	16 (13.3–51.8)	30 (19.2–54.8)	3 (2.0–4.0)	3 (2.8–5.0)
P-value	0.08	0.26	0.02	0.05	0.01	0.03
12 weeks	129 (119.5–134.5) **	120 (111.3–127.3)	14 (7.5–36.0)	27 (16.3–49.0)	2 (2.0–3.0)	3 (1.8–4.0)
P-value	0.01	0.38	0.001	0.03	0.001	0.01

*$P < 0.05$ and **$P < 0.01$ denote differences between groups analysed with Mann–Whitney *U*-test. *P*-values expressed numerically in the table denote changes within groups from baseline analysed with Wilcoxon Signed Ranks Test.

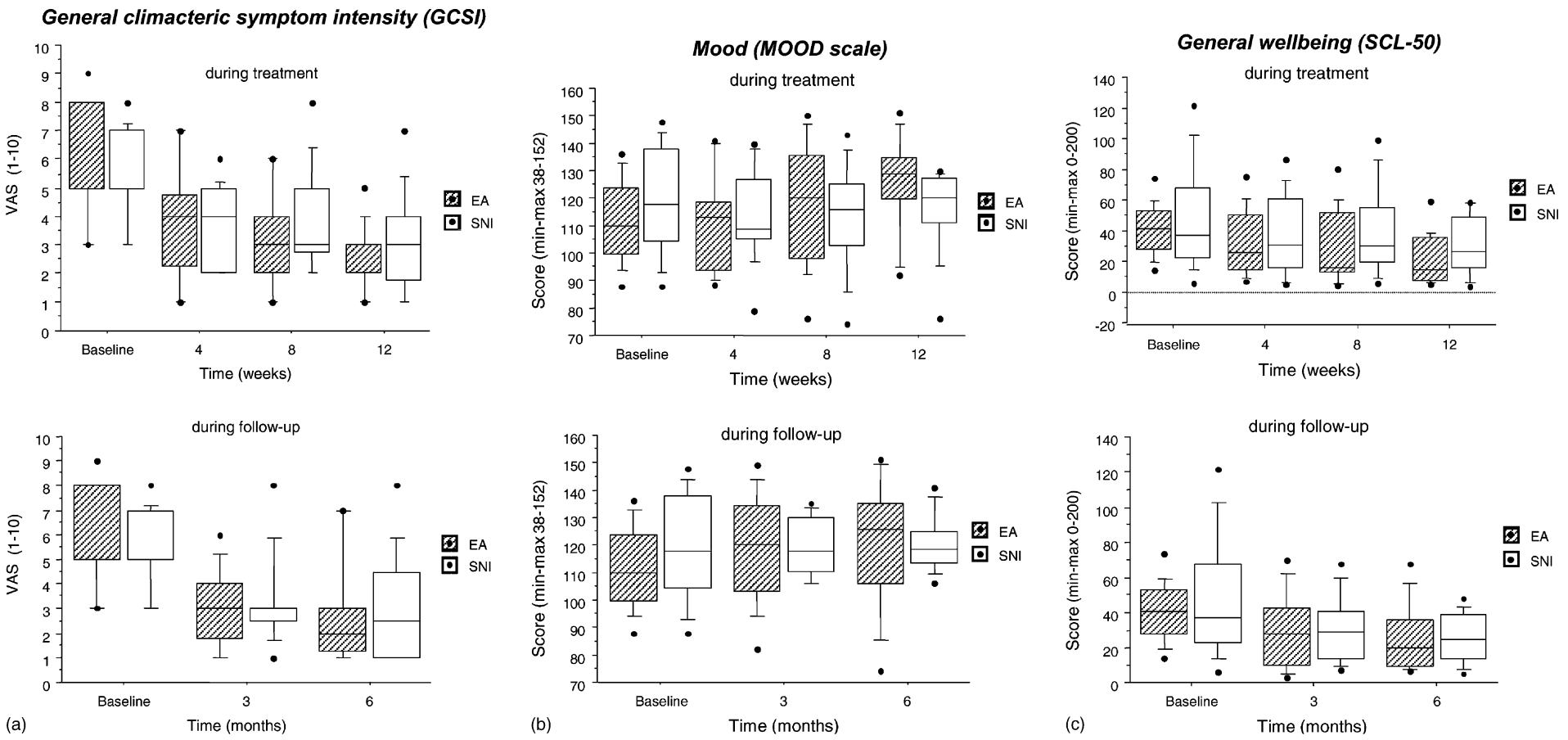

Fig. 2 (a–c) Box-plots depicting general climacteric symptom intensity (GCSI) (a), mood (MOOD Scale) (b) and general well-being (SCL-50) (c) during treatment and follow-up periods in the electro–acupuncture (EA) and superfacial needle insertion (SNI) groups. Median values with interquartile ranges, 10th and 90th percentiles, and outliers are shown.

Table 3 Results (median values with interquartile ranges, Q1–Q3) from subjective ratings of mood (MOOD Scale), psychological well-being (SCL-50) and GCSI in postmenopausal women at baseline and at follow-up 3 and 6 months after end of 12 weeks of EA and SNI

Timepoint	Variables (min–max)					
	MOOD Scale (38–152)		SCL-50 (0–200)		GCSI (VAS 1–10)	
	EA MD (Q1–Q3)	SNI MD (Q1–Q3)	EA MD (Q1–Q3)	SNI MD (Q1–Q3)	EA MD (Q1–Q3)	SNI MD (Q1–Q3)
Baseline	110 (99.8–123.8)	118 (104.0–138.0)	41 (27.5–53.3)	37 (22.8–67.8)	5 (5.0–8.0)	5 (5.0–7.0)
3 months	120 (103.3–134.0)	118 (110.5–130.0)	28 (10.3–42.0)	29 (13.5–40.5)	3 (1.8–4.0)	3 (2.5–3.0)
P-value	0.04	0.38	0.02	0.02	0.01	0.03
6 months	126 (106.3–135.3)	119 (113.5–125.0)	20 (9.8–35.8)	25 (13.9–38.5)	2 (1.3–3.0)	3 (1.0–4.5)
P-value	0.07	0.61	0.01	0.03	0.04	0.02

P-values denote changes within groups from baseline analysed with Wilcoxon Signed Ranks Test; 3 months: $n = 13$ in EA group, $n = 12$ in SNP group; 6 months: $n = 11$ in the EA group, $n = 12$ in the SNI group.

Table 4 Factors influencing non-specific responses

Patient factors	Therapist factors	Treatment factors	Environmental factors
Positive expectations	Positive expectation	'Mystique'-needles	University Hospital
Belief	Positive attitude	'Serious'-EA	Quiet
Confidence	Knowledge	Long treatment period	Warm
Learning/conditioning	Interest		Peaceful
Relaxation	Empathy		Comfortable
Anxiety reduction	Warm contact		
Stress reduction	Caring		
	Social interaction		

ergoreceptors in muscles.[6,20] Repeated EA releases endogenous opioids and oxytocin, which seem to be essential in the induction of functional changes of different organ systems.[6,15] It is suggested that hypothalamic nuclei have a central role in mediating effects of EA, such as a decreased sympathetic tone. Relaxation and improved sleep, as well as euphoria and decreased psychological tension are other changes related to EA.[6,11] In humans, morphine-like drugs produce similar changes to those produced by the endogenous opioids.[23] In animals, less irritable aggression and more calmness are shown after EA.[14,15] The specific effect of EA on mood in the present study can be compared with the results of a similarly designed study on applied relaxation in postmenopausal women, where improvements in psychological well-being and decrease of climacteric symptoms were not paralleled by improvements in mood.[24] Furthermore, in rat, the synthesis and release of serotonin and norepinephrine in the CNS accelerates following EA,[12] and in depressive patients clinical data indicate that EA may be as effective as tricyclic amitriptyline.[13] Considering these findings, it may be thought that different modulating central mechanisms evoked by repeated EA for at least 12 weeks may result in the specific improvements found on mood, and contribute to the decrease in psychological distress.

Non-specific effects

The subjective and objective non-specific, or placebo, effects induced by the therapeutic situation are well documented, and are influenced by patient, treatment, therapist and environmental factors[16,25–27] (Table 4). There are reports of placebo effects being sustained for more than 6 months, despite the general belief that placebo responses have a brief and fading action.[16,25–27] Effects on climacteric symptoms were seen early in the present study and persisted throughout the study in both groups. Moreover, in the study by Wyon et al.[5] with identically treated EA and control groups, both groups improved on number of hot flushes and 24-h urine excretion of calcitonin-gene-related peptide, without significant between-groups differences. Thus, the results of the two studies are consistent, and indicate that both psychological and physiological changes may occur.

The commonest theory, explaining the placebo responses, is the expectation of the subject, as well as the expectation, enthusiasm, interest and charisma of the therapist.[25–27] Treatment may have positive effects also because of a learning process by previous effective treatments, referred to as conditioning.[27] The unspecific effects in the present study might to some extent also depend on stress and anxiety reduction, mediated by changes in autonomic arousal. Such changes are most likely to occur in systems, which are at least partially under autonomic control,[27] like vasomotor symptoms. It is also suggested that all kinds of friendly social contact, during which non-noxious sensory stimulation is given, may induce a psychophysiological response including calmness, sedation, relaxation, decreased sympathoadrenal activity and increased vagal nerve tone, by release of endogenous oxytocin.[15,28] Moreover, social interaction and activity appear to be mediated, at least in part, by the opioid system.[29] It has also been suggested that placebo analgesia be mediated by endogenous opioids,[30] i.e. by the same mechanisms as EA.

In the present study, the women would allow themselves to relax for about 45 min once or twice a week for 3 months, which also is likely to contribute to a decrease of the sympathetic activity. They experienced a professionally warm contact and care from the therapist, as well as a peaceful, warm and quiet environment. Thus, the needling procedure was not isolated from the context in which it was performed, and certainly, this clinical approach may evoke non-specific effects. Treatments that are ostensibly more 'serious' or 'major' in some respect might be associated with a greater placebo response.[25,27] In this respect, one would expect EA to cause greater non-specific effects than the control method of SNI. Furthermore, long treatment periods in themselves have a therapeutic value.[31] Thus, several central modulating mechanisms might be involved also in the complexity of the non-specific effects found in the present study.

In conclusion, this study does not show that EA is better than extremely superficially inserted needles for the amelioration of general psychological distress and experience of climacteric symptoms in women with vasomotor symptoms after menopause. However, the more pronounced effect of EA on mood suggests that EA might have additional effects

compared with SNI. As the probability of a type II error, failing to detect an actual difference is high in small trials, large randomised controlled studies will be needed, and by including a proper waiting list control effect on variables due to time will be excluded.

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