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Clinical and biochemical observations during treatment of depression with electroacupuncture: a pilot study

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Six patients suffering from major depression were treated with electroacupuncture. During 4 weeks of treatment, the total CPRS-S-A score decreased from 23.8 to 13.4 ($p = 0.0095$). A decrease of neuropeptide Y (NPY) in plasma during the first 2 weeks of treatment was noted in five of the patients, all being women ($p = 0.0431$). The decrease was negatively correlated with age ($rs = -0.29$; $p = 0.046$). The results are in line with a putative antidepressive effect of electroacupuncture, along with an influence on NPY in plasma. Copyright © 2002 John Wiley & Sons, Ltd.

KEY WORDS — acupuncture; depression; electroacupuncture; neuropeptide Y

INTRODUCTION

The fact that 30% of depressed patients do not respond to pharmacological treatment and that side effects are common (Sitsen and Montgomery, 1994) warrants evaluation of alternative methods of treatment.

For more than 1000 years, acupuncture has been used as a treatment for somatic and mental disorders in traditional Chinese medicine (TCM) (Luo *et al.*, 1995). During the past 50 years, electric stimulation has been applied to the acupuncture needles, which appears to be more effective in the treatment of depression (Luo *et al.*, 1995).

TCM and Western medicine differ as to the principles of diagnosis and treatment. According to TCM, illness is caused by unbalanced energies in the body and between different organ systems. Applying Western scientific methods to such a medical culture is difficult (Richardson and Vincent, 1986). Nevertheless, there are some Chinese studies describing an antidepressant effect of electroacupuncture which is similar to that of amitriptyline, but with fewer side-effects (Luo *et al.*, 1985; Lou *et al.*, 1990; Luo *et al.*, 1995; Luo *et al.*, 1998).

The mechanisms of electroacupuncture are similar to those in prolonged rhythmic exercise. Muscle receptors activate A-δ fibres and thus induce a release of endorphins and serotonin (5-HT) in the brain (Thorén *et al.*, 1990). In mammals, electroacupuncture increases gene expression and the release and turnover of 5-HT (Ma *et al.*, 1992; Han, 1986). In man, the turnover of 5-HT and noradrenaline (NA) is increased while dopamine (DA) remains unaffected (Chang, 1984). Similar effects have been noted after electroconvulsive treatment (ECT), which, however, also increased DA turnover (Chang, 1984).

Neuropeptide Y (NPY) is a central and peripheral neurotransmitter considered to play a role in depression and anxiety (Bucinskaite *et al.*, 1994; Heilig *et al.*, 1994). The cerebrospinal fluid (CSF) level of NPY is reduced in depressed patients and in the brain tissue of suicide victims (Heilig *et al.*, 1994). Increased levels were found in rat brain tissue after chronic treatment with tricyclic antidepressants (TCA) (Heilig *et al.*, 1994) and after ECT or repeated electroacupuncture (Bucinskaite *et al.*, 1994).

The observation that electroacupuncture affects 5-HT, NA, NPY and endorphins, substances considered to be involved in depression, warrants an elucidation of its role in the treatment of the disorder. In the

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present pilot study, we have focused on the effect of electroacupuncture on plasma NPY.

SUBJECTS AND METHODS

Six patients, five females (aged 44.6 ± 8.0) and one male (aged 52.4) suffering from major depression according to DSM-IV (APA, 1994) were included after obtaining their informed consent. The patients were recruited through an advertisement in the local newspaper. The depression was of a moderate degree defined as a score of 10–30 on the Montgomery Åsberg depression rating scale (MADRS) (Montgomery and Åsberg, 1979). Except for depression, all patients were healthy according to the history, somatic status and basic blood tests, medication-free and not pregnant or drug abusers.

Treatment was administered using four needles, two on the head (Gv 20 and Ex 1) and two on one leg (St 36 and Bl 57). The needles were stimulated with 2 Hz at an intensity just below the pain threshold, which produced pairwise muscle contractions. The intensity was adjusted at half-time. Manual acupuncture with two needles (Pc 6 and Lr 4) was also used with stimulation at insertion, at half-time and just before the needles were taken out. The treatment lasted 25–35 min. The procedure used was according to TCM (Andersson *et al.*, 1992). Treatment was given five times a week during the first 2 weeks, three times a week during the next 2 weeks and once or twice a week during the last 2 weeks.

The patients filled in the comprehensive psychopathological rating scale self-rating scale for affective syndromes (CPRS-S-A) (Svanborg and Åsberg, 1994) before treatment, every week during treatment, and 3 and 6 months after treatment.

An experienced psychiatrist (CN) rated the depression according to the MADRS (Montgomery and Åsberg, 1979) and the Hamilton depression rating scale (HAM-D) (Hamilton, 1960) before and after 4 weeks of treatment.

Blood samples for assays of NPY were drawn before treatment and after 2, 4 and 6 weeks of treatment. The samples were placed on ice in heparin vacutainer tubes and centrifuged at 3000 rpm for 20 min at −4°C. NPY was analysed at the Clinical Chemistry Laboratory of University Hospital in Linköping using a radioimmunoassay method (Theodorsson-Norheim *et al.*, 1985).

The Statview II programme (Abucus Concepts Inc.) was used. Non-parametric tests were employed throughout (Siegel and Castellan Jr, 1988).

The study was approved by the Ethics Committee of the Linköping University Hospital.

RESULTS

Data are presented in Table 1. After 4 weeks, one patient left the study owing to insufficient improvement. For technical reasons, we could only determine NPY in plasma obtained before and after 2 weeks of treatment.

Using the Friedman two-way ANOVA on the sums of the CPRS-S-A scores before treatment and every week until week 4, a significant decrease was found ($n = 6$; $\chi^2 = 13.39$; $p = 0.0095$) (Figure 1). The significance was mainly due to six items, namely mood, feelings of unease, irritability and anger, ability to make decisions and emotional involvement (Table 1). A similar result was found for the five patients who completed 6 weeks of treatment ($n = 5$; $\chi^2 = 21.06$; $p = 0.0018$), the mean score decreasing from 23.8 (before treatment) to 10.1 at week 6.

The MADRS and HDRS scores before treatment and after 4 weeks of treatment did not differ according to the Wilcoxon signed rank test (MADRS; $n = 6$; $z = 1.80$; $p = 0.0715$; HAM-D; $n = 6$; $z = 1.78$; $p = 0.0747$).

On comparing NPY in plasma before and after 2 weeks of treatment, no difference was found in the whole group. A decrease was noted, however, in the five women (Wilcoxon signed rank test; $n = 5$; $z = -2.023$; $p = 0.0431$). Expressed as a percentage

Table 1. CPRS-S-A, MADRS and HAM-D scores (mean ± SD) before (week 0) and after 4 weeks (week 4) of electroacupuncture treatment (top panel) and NPY data (mean ± SD) before and after 2 weeks of treatment (bottom panel)

Item	Week 0	Week 4	
CPRS-S-A-items			
Mood	1.3 ± 0.7	0.4 ± 0.4	$\chi^2 = 10.9$ $p = 0.027$
Feelings of unease	1.8 ± 0.5	1.2 ± 0.6	$\chi^2 = 11.4$ $p = 0.023$
Irritability and anger	1.8 ± 0.6	0.6 ± 0.3	$\chi^2 = 16.7$ $p = 0.0022$
Ability to concentrate	2.2 ± 0.3	1.0 ± 0.8	$\chi^2 = 14.8$ $p = 0.0052$
Ability to make decisions	1.8 ± 1.0	1.0 ± 0.7	$\chi^2 = 14.8$ $p = 0.0052$
Emotional involvement	1.3 ± 0.5	0.8 ± 0.3	$\chi^2 = 11.0$ $p = 0.0092$
CPRS-S-A sum	23.8 ± 7.5	13.4 ± 8.0	$\chi^2 = 13.39$ $p = 0.0095$
MADRS sum	24.3 ± 8.2	15.0 ± 8.7	$z = 1.802$ $p = 0.0715$ n.s.
HAM-D sum	19.5 ± 6.2	10.2 ± 6.4	$z = 1.782$ $p = 0.0747$ n.s.
	Week 0	Week 2	
NPY sort	38.0 ± 16.3	31.1 ± 11.8	$z = 2.023$ $p = 0.0431$

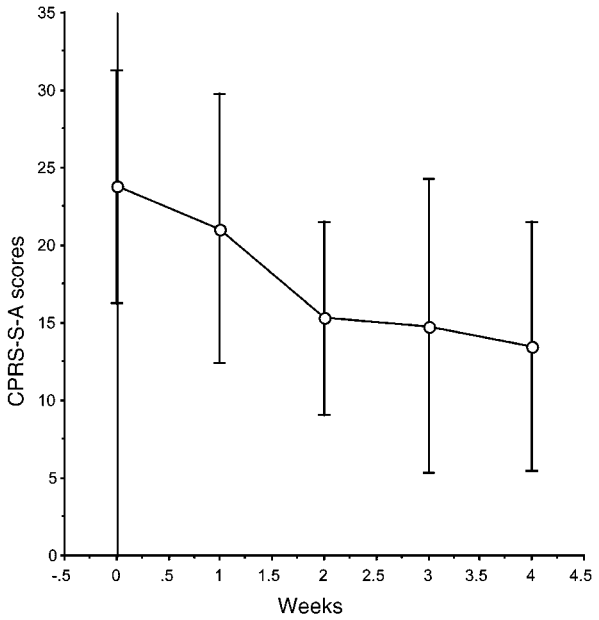

Figure 1. Sum of CPRS-S-A scores (mean ± SD) of six depressed patients treated with electroacupuncture during 4 weeks ($n = 6$; $\chi^2 = 13.39$; $p = 0.0095$)

of the pretreatment level, NPY after 2 weeks of treatment decreased with increasing age (Spearman rank correlation; $n = 5$; $r_s = -0.29$; $p = 0.046$) (Figure 2).

DISCUSSION

The reduction in the CPRS-S-A score (Figure 1) is in line with an antidepressant effect of electroacupuncture, mainly consisting of changes in six items (Table 1). Two items of specific importance in depression, mood and emotional involvement (Svanborg and Åsberg, 1994), are among the most changed ones. Other items of relevance are irritability and anger, ability to concentrate and emotional involvement (Table 1), which is in line with previously reported effects of electroacupuncture on anxiety somatisation and cognitive process disturbance (Lou *et al.*, 1990; Luo *et al.*, 1998).

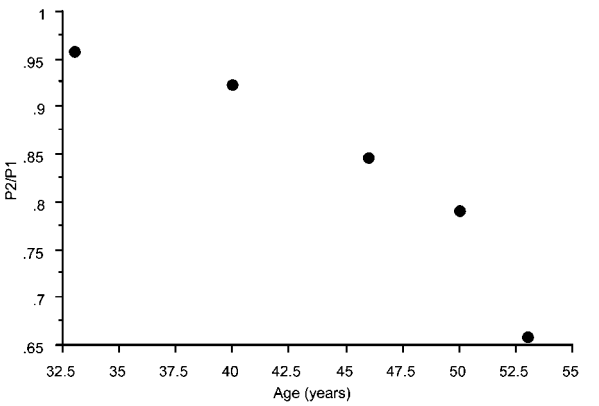

Figure 2. Relationship between NPY after 2 weeks of treatment as a percentage of pretreatment level and age (Spearman test; $n = 5$; $r_s = -0.290$; $p = 0.046$)

In contrast to the reduction of the CPRS-S-A score, based on weekly ratings, no changes were noted in MADRS and HAM-D. One reason might be that reported and apparent sadness have different biological correlates, at least concerning NA (Nordin, 1988). Another reason may be that factors such as sleep and appetite are more dominant in MADRS and HAM-D than in the CPRS-S-A (Montgomery and Åsberg, 1979; Hamilton, 1960; Svanborg and Åsberg, 1994).

Electroacupuncture may act as a mild ECT as it increases the levels of 5-HT, NA (Chang, 1984) and NPY in the brain (Bucinskaite *et al.*, 1994). Whether or not the present amelioriation is related to these biochemical correlates is not known.

We observed a decrease of NPY in plasma in the five women during the first 2 weeks of more intensive treatment (five times a week). As electroacupuncture causes a decrease in the sympathetic outflow for several hours after treatment and as peripheral NPY is usually released together with NA in sympathetic nerves, this is a possible explanation of the decrease. Whether NPY levels in the CSF and plasma correlate is, however, an open question.

It is difficult to use a proper control group in an acupuncture study and the placebo-effect cannot be ignored in a treatment with an aura of eastern mysticism (Baldry, 1993). On using electroacupuncture, a control group can be treated with manual acupuncture. It is also possible to use superficial needles placed on anathomic places not supposed to be effective in the treatment of depression ('sham acupuncture'). Notable effects have, however, been observed even in such control groups (Baldry, 1993). Furthermore, exposing depressed patients to a potentially ineffective acupuncture treatment might have ethical implications. Therefore, the present results favour conducting a larger randomised study comparing the clinical and biochemical effects of electroacupuncture with those of pharmacological treatment.

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