

Research report

# The benefit from whole body acupuncture in major depression

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Received 22 January 1998; received in revised form 31 January 1999; accepted 22 March 1999

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## Abstract

**Background:** In a single-blind placebo-controlled study design we investigated the efficacy of acupuncture additionally applied to drug treatment in major depression. **Methods:** We randomly included 70 inpatients with a major depressive episode in three different treatment groups: verum acupuncture, placebo acupuncture and a control group. All three groups were pharmacologically treated with the antidepressant mianserin. The verum group received acupuncture at specific points considered effective in the treatment of depression. The placebo group was treated with acupuncture at non-specific locations and the control group received pharmacological treatment plus clinical management. Acupuncture was applied three times a week over a period of 4 weeks. Psychopathology was rated by judges blind to verum/placebo conditions twice a week over 8 weeks. **Results:** Patients who experienced acupuncture improved slightly more than patients treated with mianserin alone. **Conclusions:** Additionally applied acupuncture improved the course of depression more than pharmacological treatment with mianserin alone. However, we could not detect any differences between placebo and verum acupuncture. © 2000 Elsevier Science B.V. All rights reserved.

**Keywords:** Acupuncture; Depression; Mianserin

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## 1. Introduction

In various different records and books acupuncture (Mann, 1973; Zhang, 1988; Bullock et al., 1989; Youbang and Liangyue, 1989), an ancient Chinese art of healing, is considered to alleviate or cure physical or mental diseases by simply piercing the skin with a fine needle at defined acupuncture points. In detail, symptoms of depression reoccur frequently

in traditional Chinese works (Hubei Zuhonggyi Xueyuan, 1979; Nguyen Van Nghi, 1983) as well as newer literature on acupuncture (Porkert, 1983; Ross and Zang, 1985; Requena, 1989; Ots, 1990), suggesting whole body acupuncture is beneficial in the treatment of depressive patients.

The present study was designed to explore the efficacy of acupuncture in treating depression. Up to now, a single placebo-controlled clinical study of acupuncture as a treatment for depression has been reported. Yang et al. (1994) published data on acupuncture employed in the case of 41 patients suffering from various types of depression. The

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diagnostic assignment was quite heterogeneous ranging from bipolar affective disorders and dysthymia to involuntal depression of in- and outpatients. One group received acupuncture with individually determined needle points, the controls were pharmacologically treated with amitriptyline ranging between 150 and 300 mg/day. After 6 weeks no significant difference in psychopathology between the two methods of treatment was found, suggesting acupuncture to be as effective as antidepressant medication.

The aim of our study was to evaluate the efficacy of whole body acupuncture additionally applied to drug treatment of depression in a single-blind placebo-controlled study design. The hypotheses tested were: (a) additionally applied acupuncture improves the course of the illness more than pharmacological treatment by itself; (b) the effect of needling defined acupuncture points is specific, meaning in the case of verum acupuncture, the improvement of the course of depression is much higher than in the case of placebo acupuncture.

## 2. Methods

### 2.1. Study design

From October 1993 to October 1995 we studied 70 consecutive inpatients suffering from a major depressive episode and randomly assigned the patients to one of three different treatment groups:

1. mianserin treatment (90–120 mg/day);
2. mianserin treatment (90–120 mg/day) plus verum acupuncture; and
3. mianserin treatment (90–120 mg/day) plus placebo acupuncture.

In all treatment groups a benzodiazepine comedication up to 20 mg/day diazepam was allowed if required. The criteria for inclusion into the study were: cross-sectional diagnosis of a major depressive episode according to DSM-III-R (American Psychiatric Association, 1987), a score  $\geq 18$  points on the 21-item Hamilton depression scale (HAMD, Hamilton, 1976), and age of the patients between 20 and 70 years. Entry into the study was limited to patients without acute suicidality, longitudinal diagnosis of

schizoaffective or bipolar affective disorder as well as delusions. Furthermore, patients with coagulation-disease, wound healing disease, emphysematous thorax, abnormal blood cell count, serious liver and kidney diseases, and epilepsy were excluded.

Because of the wide range of age for participants, we selected mianserin as the standardized antidepressant medication, which is not accompanied by anticholinergic side effects (Swinkels and de Jonghe, 1995). The dosage regimen was 30–30–30 or 30–30–60 mg/day. Written informed consent was obtained from all patients.

Psychopathology was rated at entry to the study and twice a week over a period of 8 weeks by two independent experienced judges not informed about verum/placebo acupuncture. The following observer rating scales were used to determine the psychopathological course of the illness: Global assessment scale (GAS, Endicott et al., 1976), Bech–Rafaelsen Melancholia scale (BRMS, Bech and Rafaelsen, 1980), Clinical global impressions scale (CGI, National Institute of Mental Health, 1976). For evaluation of depressive states in longitudinal studies we employed a self-rating scale (Bf-S, von Zerssen et al., 1974).

### 2.2. Subjects

Table 1 summarizes the age, gender and psychiatric diagnosis according to DSM-III-R of the patients participating in the study. The DSM-III-R number 296.2 represents a single episode, 296.3 a recurrent episode of a major depressive disorder.

### 2.3. Acupuncture protocol

Acupuncture was practised by two clinicians experienced in traditional Chinese acupuncture. They were excluded from the clinical management. For both groups, verum and placebo acupuncture, each patient was treated with a standardized whole body acupuncture treatment, applied three times a week over four consecutive weeks at 18 different locations. The duration of each acupuncture session was nearly 30 min. Each individual patient was needled over the treatment period by the same clinician. However, both clinicians did the acupuncture in both groups. The distribution verum/placebo acupuncture

Table 1  
Psychopathological characteristic of the patients according to DSM-III-R

Control-group			Verum acupuncture			Placebo acupuncture		
DSM-III-R	Age	Sex	DSM-III-R	Age	Sex	DSM-III-R	Age	Sex
296.3	28	m	296.3	44	f	296.3	55	f
296.3	64	f	296.3	51	m	296.2	45	f
296.3	65	f	296.3	56	f	296.3	50	f
296.2	53	m	296.3	32	f	296.2	32	f
296.3	53	m	296.3	68	f	296.3	36	m
296.2	44	f	296.2	44	m	296.2	53	m
296.2	32	m	296.3	57	f	296.3	56	f
296.2	36	f	296.3	55	f	296.2	65	m
296.3	47	m	296.3	65	f	296.3	41	m
296.2	47	f	296.3	35	f	296.3	56	f
296.3	59	f	296.3	64	f	296.2	49	f
296.2	38	m	296.3	53	f	296.3	55	m
296.3	63	m	296.3	53	f	296.2	63	m
296.2	58	f	296.3	21	f	296.3	52	f
296.2	38	m	296.2	65	f	296.3	42	f
296.2	53	f	296.3	50	f	296.2	32	f
296.3	63	f	296.3	26	m	296.3	44	f
296.2	59	f	296.2	41	f	296.3	44	m
296.2	41	f	296.3	30	f	296.2	54	m
296.3	59	m	296.3	53	f	296.3	38	f
296.3	53	f	296.3	51	f	296.2	45	f
296.3	53	m	296.3	55	f	296.3	43	m
296.3	42	f	–	–	–	296.2	33	f
296.3	37	f	–	–	–	296.2	50	f

was equal for both clinicians. In case of verum acupuncture we needled bilaterally at the positions: U.B.15, U.B.17, U.B.18 (back), H7 (wrist), P6 (forearm), St40 (lower leg), Sp5, Sp6 (foot), and Lu1 (upper part of the body). Skin was pierced at the acupuncture points with a fine stainless steel needle (0.3 × 25 mm) to a depth of a few millimeters which was withdrawn after the lapse of a few minutes (Nguyen Van Nghi, 1983; Ross and Zang, 1985; Bullock et al., 1989). The electric skin resistance was measured to accurately determining the acupuncture points where resistance was reduced. In the case of placebo acupuncture we needled at non-specific locations in the neighbourhood of the loci cited above merely pricking the skin superficially.

#### 2.4. Statistical analysis

Values in tables are presented as means ± S.D. Categorical variables were analyzed by means of  $\chi^2$ -tests. Baseline differences were evaluated with

one-way ANOVA. Between group differences in outcome parameters were analyzed following an intention-to-treat-analysis with repeated measures ANOVA using treatment as between subjects factor (control vs. placebo vs. verum acupuncture) and assessments 1–16 (week 1–8) as repeated measures. For adjustment of degrees of freedom due to heterogeneity of variance–covariance matrices the procedure of Huynh and Feldt (1976) was applied. The level of statistical significance was set at  $\alpha = 0.05$ .

### 3. Results

#### 3.1. Patients' characteristics

Table 2 summarizes the number of patients, gender, mean age and the HAMD score at the beginning of the study for the different treatment groups. According to  $\chi^2$ -test (gender) and ANOVAs (age, HAMD), no differences between the groups under study could be found. It is obvious that all

Table 2  
Number, sex ratio, mean age and HAMD score of the patients

Group	Number	Male:female	Mean age	HAMD
Control group	24	10:14	49±11	28±7
Verum acupuncture	22	3:19	49±13	28±5
Placebo acupuncture	24	9:15	47±9	29±5

patients suffered from a severe depression (mean score on HAMD = 28). An additionally applied one-way ANOVA did not show any difference in the number of former hospitalizations between the groups. Thus, the distribution of the patients' severity score, age, and gender ratio was quite homogeneous across the groups.

### 3.2. Differences between the three different treatments under study

Figs. 1–5 show the course of the depression according to the observer rating scales GAS, BRMS, CGI, and the self rating scale Bf-S over a time period of 8 weeks. In all cases there was greater improvement when acupuncture (placebo or verum) was applied compared to plain pharmacological treatment. In case of GAS (the higher the score, the better the psychopathology) the different groups under study improved homogeneously within the first 4 weeks of treatment (Fig. 1). However, during the

last 4 weeks patients who had experienced acupuncture reached a higher score than patients treated with mianserin alone. For the observer ratings BRMS and CGI, respectively, again the three groups improved equally during the first half of the study (the lower the scores the better the psychopathology), whereas during the second half patients previously treated with acupuncture showed greater benefit (Figs. 2–4). According to the self rating scale Bf-S (the lower the score the better the psychopathology) we observed the same course of depression over time: patients who had experienced acupuncture showed more rapid progress than patients with mianserin alone (Fig. 5).

For each rating instrument Table 3 summarizes the results of the two-way ANOVA with between-subjects factor group (control vs. placebo vs. verum acupuncture) and within-subject factor time (repeated measure design of ratings 1–16). We could not detect any statistically significant main effect for the factor group, but in all instruments a highly significant

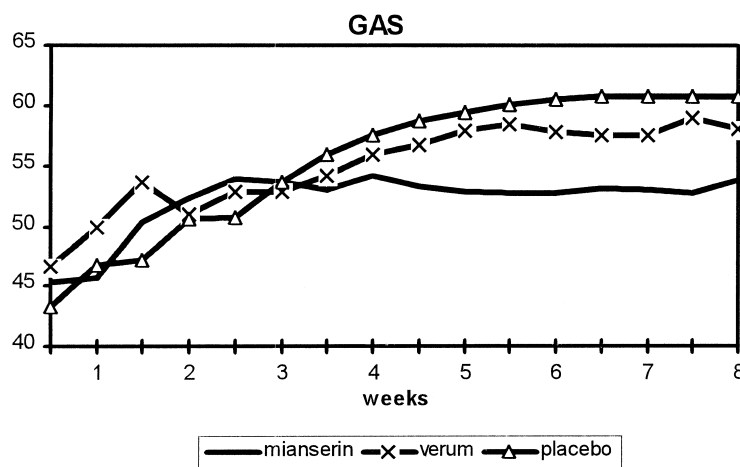


Fig. 1. GAS ratings (global assessment) over time (the better the score, the better the psychopathology).

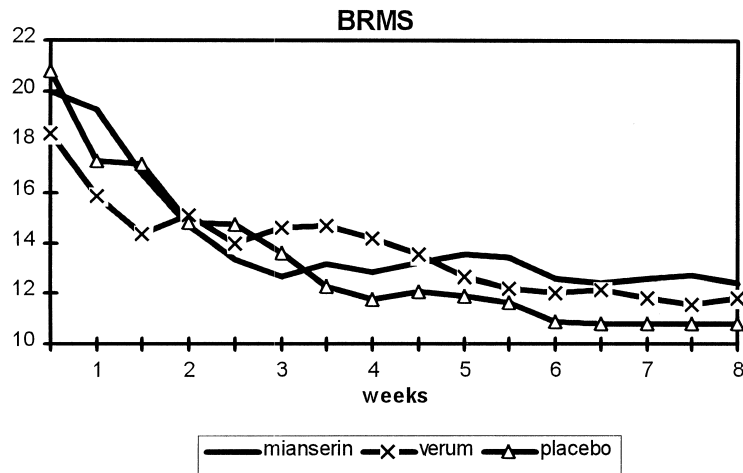


Fig. 2. BRMS ratings (melancholia scale) over time (the lower the score, the better the psychopathology).

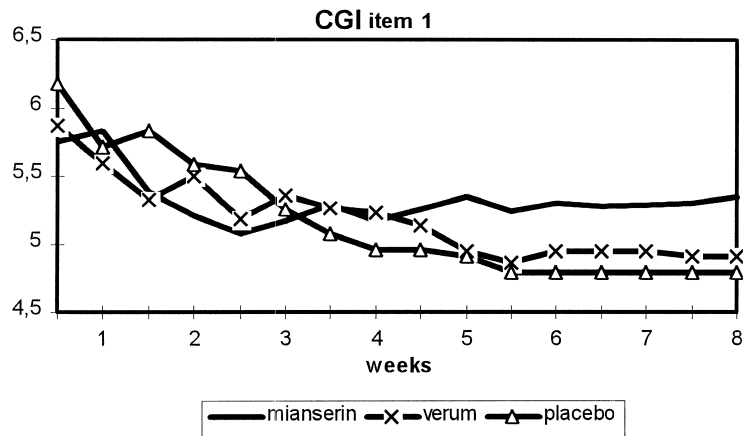


Fig. 3. CGI ratings (item 1 = psychopathological state) over time (the lower the score, the better the psychopathology).

effect for the factor time. In case of CGI item 2 (measuring the improvement of psychopathology) we found a statistically significant interaction of group by time ( $P = 0.048$ ).

Additionally, we investigated the differences in mianserin dosage and diazepam comedication (if required) between the three treatment groups. Fig. 6 shows the mianserin medication and the diazepam dosage during the study period. Table 4 summarizes the results of a two-way ANOVA for both mianserin and diazepam. No main effect for the factor group

nor any statistically significant interaction of group by time could be observed. Thus, the significant interaction of group by time for CGI (item 2) is not due to influence by different medication.

### 3.3. Differences between control and acupuncture treatment

In order to detect differences between the drug treatment and both acupuncture conditions (placebo as well as verum acupuncture), we performed a

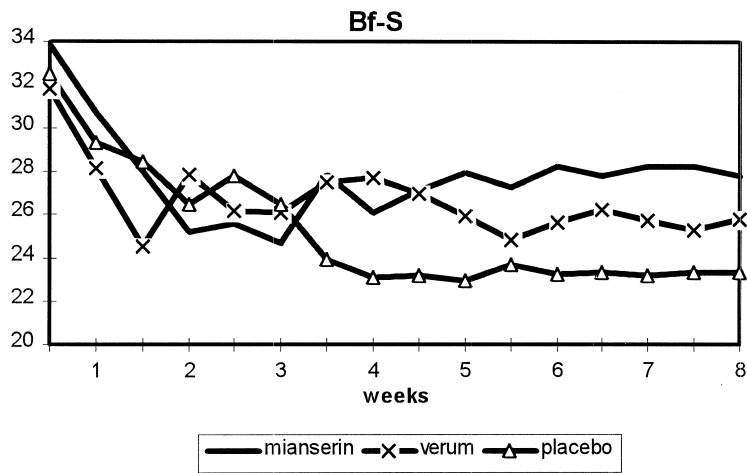


Fig. 5. Bf-S self ratings (depressive mood) over time (the lower the score, the better the psychopathology).

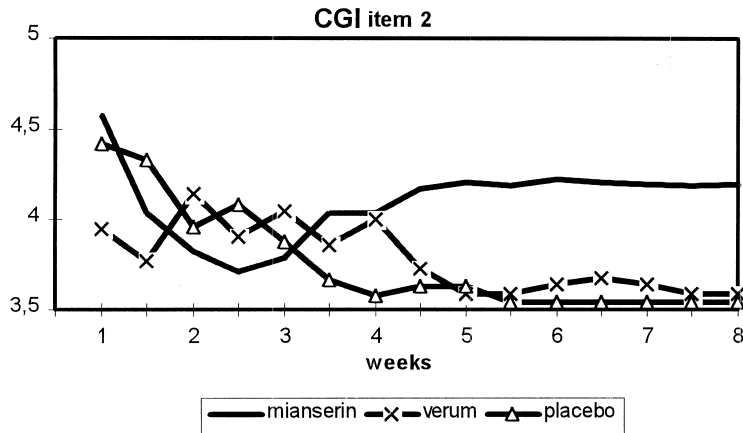


Fig. 4. CGI ratings (item 2 = improvement) over time (the lower the score, the better the psychopathology).

Table 3  
Summary of two-way ANOVA for each of the rating instruments (Huynh–Feldt adjusted *P* values)

Instrument	ANOVA (between the three treatment groups)		
	Group	Time	Interaction
CGI item 1	$F_{2,67} = 0.12$ $P = 0.889$	$F_{15,1005} = 12.36$ $P = 0.0001$	$F_{30,1005} = 1.94$ $P = 0.092$
CGI item 2	$F_{2,67} = 0.84$ $P = 0.435$	$F_{15,1005} = 48.23$ $P = 0.0001$	$F_{30,1005} = 2.36$ $P = 0.048$
BRMS (sumscore)	$F_{2,67} = 0.10$ $P = 0.906$	$F_{15,1005} = 23.79$ $P = 0.0001$	$F_{30,1005} = 1.39$ $P = 0.226$
GAS	$F_{2,67} = 0.65$ $P = 0.525$	$F_{15,1005} = 19.18$ $P = 0.0001$	$F_{30,1005} = 2.16$ $P = 0.052$
Bf-S	$F_{2,67} = 0.25$ $P = 0.782$	$F_{15,1005} = 4.99$ $P = 0.0001$	$F_{30,1005} = 1.22$ $P = 0.296$

two-way ANOVA with between-subject factor group (control vs. acupuncture) and within-subject factor time. Table 5 summarizes the results. No main effect for the factor group could be found. However, for the instruments CGI (item 2) and GAS statistically a significant interaction was shown.

Therefore, according to the observer ratings CGI (item 2) and GAS patients treated with acupuncture (placebo or verum) showed higher benefit than patients treated only with mianserin. However, we could not detect any difference between patients who had experienced verum acupuncture and those who had placebo acupuncture. A two-way ANOVA with

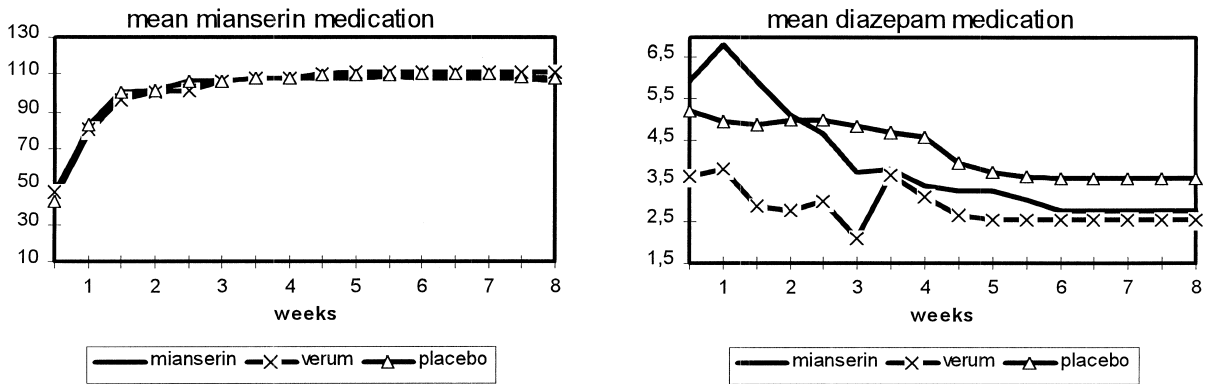


Fig. 6. Mianserin and diazepam medication during the study period.

Table 4  
Results of ANOVA for mianserin and diazepam medication

Medication	ANOVA (between the three treatment groups)		
	Group	Time	Interaction
Mianserin	$F_{2,67} = 0.06$ $P = 0.940$	$F_{15,1005} = 201.28$ $P = 0.0001$	$F_{30,1005} = 0.65$ $P = 0.693$
Diazepam	$F_{2,67} = 0.70$ $P = 0.502$	$F_{15,1005} = 6.07$ $P = 0.001$	$F_{30,1005} = 1.25$ $P = 0.288$

Table 5  
Results of the ANOVA with between-subject factor group (control vs. acupuncture) and within-subject factor time (Huynh–Feldt adjusted  $P$  values)

Instrument	ANOVA (mianserin versus both acupuncture groups)		
	Group	Time	Interaction
CGI item 1	$F_{1,68} = 0.24$ $P = 0.628$	$F_{15,1020} = 8.95$ $P = 0.0001$	$F_{15,1020} = 2.63$ $P = 0.065$
CGI item 2	$F_{1,68} = 1.71$ $P = 0.195$	$F_{15,1020} = 44.60$ $P = 0.0001$	$F_{15,10200} = 3.14$ $P = 0.026$
BRMS (sumscore)	$F_{1,68} = 0.15$ $P = 0.702$	$F_{15,1020} = 21.64$ $P = 0.0001$	$F_{15,1020} = 1.09$ $P = 0.348$
GAS	$F_{1,68} = 1.30$ $P = 0.257$	$F_{15,1020} = 14.20$ $P = 0.0001$	$F_{15,1020} = 3.03$ $P = 0.049$
Bf-S	$F_{1,68} = 0.35$ $P = 0.558$	$F_{15,1020} = 4.21$ $P = 0.005$	$F_{15,1020} = 1.14$ $P = 0.336$

factor group (placebo vs. verum acupuncture) and within-subject factor time did not come out with any statistically significant main effect for the factor group or any significant interaction. Therefore, we could demonstrate an improvement of the depressive

psychopathology when acupuncture had been applied, but this effect appeared to be nonspecific.

### 3.4. Responder analysis

According to GAS scale we defined a low improvement when GAS score at the end of the study was less than 25 points above the baseline value. A medium or high improvement was defined when GAS score at the end was more than 25 points above baseline value. Following this definition we observed a statistically significant difference between the three groups under study ( $\chi^2 = 6.75$ ,  $df = 2$ ,  $P = 0.034$ ). Comparing placebo and verum acupuncture we could not detect any significant difference in responder rate. However, comparing both verum and placebo acupuncture with control conditions we found a higher responder rate in case of acupuncture ( $\chi^2 = 5.01$ ,  $df = 1$ ,  $P = 0.025$ ). Table 6 summarizes the responder rate for control, placebo, and verum conditions.

Table 6  
Responder analysis according to GAS score

GAS	Control group	Verum acupuncture	Placebo acupuncture
No or low improvement ( $\leq 25$ points)	$n = 23$ 96%	$n = 18$ 82%	$n = 16$ 67%
Medium or high improvement ( $> 25$ points)	$n = 1$ 4%	$n = 4$ 18%	$n = 8$ 33%

#### 4. Discussion

In this single-blind placebo-controlled study we investigated the effectiveness of additionally applied whole body acupuncture in the treatment of severe depression. For this reason three different treatment procedures were selected, having a standardized pharmacological treatment with mianserin in common. The first group experienced verum acupuncture with needling points, which are proposed for the treatment of depressive symptoms (Mann, 1973). In the second group placebo acupuncture was applied with needling points not being regarded as any specific acupuncture locations and not inserted in the recommended depth. In the third group (control) we did not apply any acupuncture technique. The first hypothesis tested could be confirmed: additionally applied acupuncture did improve the course of depression more than pharmacological treatment with mianserin did by itself. The second hypothesis, however, had to be rejected: we could not detect any differences between placebo and verum acupuncture. Thus, our results point to the view that there is no specific effect of needling defined acupuncture points in the treatment of major depression (Wolf et al., 1995).

This outcome did not correspond to a ceiling effect due to highly sufficient pharmacological medication. In each treatment group the patients suffered from a severe major depressive disorder according to DSM-III-R. During the study period of 8 weeks the patients did not experience a full remission, neither in the control group nor in the acupuncture groups. Therefore, the medication dosage chosen did not appear highly potent and verum acupuncture should have shown a measurable improvement if effective. However, patients additionally treated with either verum or placebo acupuncture experienced a statistically significant higher benefit than patients in the control group. There was no difference in mianserin dosage or diazepam comedication between the groups. The responder rate was higher when acupuncture was applied and the differences observed did not depend on different numbers of drop-outs. A more complete analysis revealed a complete rate of the acupuncture groups in the same order as under control conditions. One might discuss whether our placebo condition was really placebo (Patell, 1987;

Vincent and Lewith, 1995). It might be the case that the effect of acupuncture does depend on the needling itself and that it is not necessary to needle specific acupuncture locations.

Another reason for the missing effectiveness and superiority of verum acupuncture might be the severity of depression and the operationally defined major depressive episodes according to DSM-III-R criteria, which, of course, were not subject to traditional Chinese proposals in the treatment of mood disorders. It is not excluded that needling of other points would come out with other results. Particularly from the traditional point of view it appears suitable to needle individually selected points for each patient and not performing a standardized acupuncture design as presented here.

The results of our study suggest that the effect of acupuncture is unspecific and might be due to additional attention provided three times a week for nearly half an hour. Patients under acupuncture treatment experienced a calm environment with a high degree of relaxation. Moreover, we cannot exclude that the clinicians performing the acupuncture and necessarily being informed about verum and placebo conditions, intensively cared for in particular the patients receiving placebo acupuncture. This phenomenon might explain why patients under placebo acupuncture improved slightly more than those under verum conditions.

#### Acknowledgements

This work was supported by Rut- und Klaus-Bahlsen-Stiftung, Germany. It contains essential parts of the doctoral dissertation of S. Bech.

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