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Acupuncture and anxiety 2013: The year in (literature) review.

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Abstract: A Pubmed search yielded 20 studies involving acupuncture and anxiety published in 2013. This paper reviews these studies. A variety of methods and populations were explored. A number of methodological flaws compromised the validity of much of the research. The paper gives suggestions for improving the quality of research done in this area in the future.

Keywords: Acupuncture, Anxiety, literature review

A PubMed search of keywords “Acupuncture” and “Anxiety” yielded 42 matches. Of these, ten were literature review and did not report any new studies, three reported non-acupuncture interventions, three were editorials, four were not related to acupuncture’s effect on anxiety, one was a proposed study protocol, and one was a report from a placebo conference. This left 20 new studies on the topic of Acupuncture and Anxiety to review.

Unless otherwise specified, subjects were randomized into their treatment arms; the treatment arms were statistically similar at baseline, and clinical findings were statistically significant to $p \leq 0.05$.

The ability of acupuncture to treat anxiety has been documented. It has been shown effective in treating: Generalized anxiety, depressive anxiety, pre-operative anxiety, and more. Pilkington et al authored an excellent review on this subject (1). While anxiety is its own problem, it can also increase an individual’s susceptibility to other diseases (2). Much acupuncture research is now adding anxiety assessments to their protocol. These assessments are easy to administer and are useful in helping identify what sort of interventions are most effective in treating anxiety. In the past year, researchers looked at new point protocols and new populations.

Carvalho et al (3) studied the effect of acupuncture on anxiety and depression caused by premenstrual dysphoric disorder. They split 26 women into two groups (true and sham) and assessed them before and after a course of treatment with the Hamilton Anxiety (HAM-A) and Hamilton Depression (HAM-D) Rating Scales. Both groups were treated twice weekly over two menstrual cycles (16 treatments total). Treatment group had needles inserted at Neiguan PC6, Taichong Lv3, Yanglingquan GB34, Hegu LI4, Waiguan TW5, and Sanyinjiao Sp6, retained for 30 minutes after obtaining deqi. In the sham group, needles were inserted shallowly at points 2cm away from the points used in the treatment group and quickly removed without the patients’ knowledge. There is now sufficient evidence to show that sham acupuncture is not a true placebo because it is not inert and does have effects similar to true acupuncture (4). Even so, this study showed true acupuncture’s superiority. Subjects in the sham group saw their anxiety drop by 21% while subjects in the treatment group had their anxiety reduced by 59%. In addition, subjects in the sham group had depression reduced by 19% and subjects in the treatment group had it reduced by 52%.

Reshef et al (5) studied the effect of acupuncture on patients with schizophrenia in a pilot study. Their primary focus was sleep, but they also examined anxiety and depression. Twenty patients diagnosed with schizophrenia or schizoaffective disorder were evaluated at baseline and after eight weeks of twice-weekly acupuncture. Sleep was measured by a wrist actigraph and subjective questionnaires. Anxiety was measured by the State Trait Anxiety Inventory (STAI), and the HAM-A. After eight weeks, many parameters of sleep were improved and anxiety and depression were lessened significantly according to all measures. Two limitations of this study are that 1) there was no control group; and 2) each patient received individualized treatment and the points used were not reported.

McPhearson and McGraw (6) studied a multi-therapy approach to reducing anxiety. 37 volunteers at a military facility received six weeks of acupuncture at Shenmen Ht7, Zusanli St36, Yintang Ex-HN-3, Taixi Kd3, and Taichong Lv3. Additional points at Qihai CV6, Jueque CV14, Sanyinjiao Sp6, and Hegu LI4 were added at the provider's discretion. The length and frequency of treatments were not specified in the report. Additional therapies were utilized by subjects including: yoga, dietary changes, journaling, aromatherapy, and breathing exercises. Anxiety was measured pre- and post-intervention via the Depression Anxiety Stress Scale-21 (DASS-21) and the Generalized Anxiety Disorder-7 item scale (GAD-7). Clinical improvements were found in depression, anxiety, stress, and the use of anxiolytic medication. But since the approach was multi-faceted and lacked a control group, it is impossible to evaluate how much, if at all, the acupuncture protocol contributed to the improvement.

Lu and Lu (7) compared the effectiveness of different single acupoints. They studied 108 subjects with a history of panic attacks and phobias regarding medical or dental procedures and who's anxiety prevented them from hypnotic induction. Each patient received acupuncture at either Hegu LI4, Shenmen Ht7, Anmian EX-HN-8, Neiguan PC6, Sanyinjiao Sp6, or Yintang Ex-HN-3. Anxiety was measured by pulse, blood pressure, and blood oxygenation. They found that Yintang Ex-HN-3 was most effective at helping subjects enter into hypnosis, Hegu LI4 was most effective at relaxing muscles and reducing pain, and Shenmen Ht7 was most effective at pulse reduction. Investigators suggest that Yintang's Ex-HN-3 effectiveness was through improving subjects' concentration on the hypnotist's instructions. All of the points investigated helped some of the subjects fall into a hypnotic state and undergo procedures that they had previously been unable to tolerate.

Wang et al (8) examined the effect of electro acupuncture (EA) on personality traits in depression and compared it to the effect of Paroxetine HCl (Paxil). They used the Minnesota Multiphasic Personality Inventory (MMPI), Self-rating Anxiety Scale (SAS), Self-rating Depression Scale (SDS), and the Montgomery-Asberg Depression Rating Scale (MADRS). Subjects were needled at Baihui GV20, Sishencong Ex-HN-1, Shenmen Ht7, and Sanyinjiao (Sp6) with EA at Yintang Ex-HN-3 and Neiguan PC6. EA utilized 125 ms intermittent pulse at 40 Hz. Deqi was achieved; treatments lasted for 20 minutes and were administered three times per week for 24 weeks. Control group took paroxetine for 24 weeks. The authors reported that depression, paranoia, and social introversion were reduced more for the acupuncture group than the paroxetine group; but

the reduction in anxiety was similar in both groups.

Smith et al (9) compared acupuncture to acupressure control in the treatment of anorexia nervosa with 26 inpatients. They utilized Hegu LI4, Neiguan PC6, Yanglingqian GB34, Taichong Lv3, and Zusanli St36 in both groups, and additional points were added according to each patient's TCM diagnosis (although these points and the criteria for determining a TCM diagnosis were not specified in the report). Body Mass Index (BMI) was the primary measure, but they also examined anxiety via the Depression Anxiety Stress Scale (DAS). Subjects received 9 treatments during their 6-week inpatient stay. While both groups experienced reductions in the anxiety level, the reduction in anxiety was not significant nor was the difference between the two interventions.

On the biochemical level, Zhao et al (10) examined the chemical changes that anxiety causes in rat's brains and acupuncture's effect on moderating those effects. They addicted mice to ethanol. Then they removed access to ethanol for three days. On each of those days, the rats received one minute of acupuncture either at: Shenmen Ht7, Neiguan PC6, or a non-acupoint on the tail. Rats were observed on a elevated plus maze (EPM) to assess anxiety before their brains were analyzed. Radioimmunoassay was performed to quantify the Corticotropin-Releasing Factor (CRF) content of the center nucleus of the amygdala. They also tested plasma levels of Corticosterone (CORT). Through the use of multiple control arms, they showed that A) Ethanol withdrawal increases CRF and CORT, B) The increased CRF and CORT were associated with increased anxiety on the EPM, C) Acupuncture at Shenmen Ht7 prevented these increases (while other points did not), and D) Reintroduction of CRF directly into the amygdala caused the anxiety to return in the Shenmen Ht7 group. This reinforced the data showing that CRF and CORT are important compounds in mediating stress response and showed that Shenmen Ht7 affects their actions in vivo.

Bussell studied the effect of acupuncture on working memory (WM) and anxiety (11). Since acupuncture has been shown to reduce anxiety, and anxiety has been shown to impair WM, the hypothesis was that acupuncture could improve WM by reducing anxiety. 90 undergraduate subjects completed the STAI then were split into acupuncture and control groups. Acupuncture group had needles inserted into Sishencong Ex-HN-1, Shenting Du24, Yintang Ex-HN-3, Neiguan PC6, Shenmen Ht7, and Taixi Kd3. There was no requirement that deqi was obtained. Control subjects had the same points touched and swabbed but no needles were inserted. The amount of verbal and physical contact was kept consistent between groups. All subjects laid on a treatment table for 20 minutes. Then they all took the state-portion of the STAI again and the Automated Operation Span Task- a computerized test of working memory. This protocol significantly improved WM recall by 9.5% and reduced processing errors by 36% compared with control. Acupuncture subjects also had significantly lower state anxiety than control, but the effect on WM and anxiety were unrelated. It was not the case that those with the lowest anxiety performed best on the AOSPAN, nor was it the case that those with the greatest drop in anxiety performed best. This protocol improved WM and reduced anxiety but those effects were independent.

Arvidsdotter, Marklund, and Taft (12) studied 120 subjects who were seeking treatment for psychological distress. 40 subjects were assigned to each group: Conventional Therapy (CT), Traditional Acupuncture (TA), and Integrative Treatment (IT). All subjects were treated once a week for 8 weeks. CT included psychotherapy or watchful waiting. TA utilized Baihui GV20, Qihai CV6, Neiguan PC6, Shenmen Ht7, Hegu LI4, Taichong Lv3, Sanyinjiao Sp6, Zusanli St36, and additional ashi points, with deqi, retained for 20-30 minutes. IT group received TA and salutogenic therapy. Anxiety and depression were measured by the Hospital Anxiety and Depression Scale (HADS) at baseline; and after four and eight weeks of treatment. There was improvement in both the IT and TA groups compared to the CT group at four and eight weeks, but there was no difference between IT and TA groups.

Lima, Ferreira, and Pace (13) examined the effect of acupuncture on 30 subjects with dyspepsia; but they also used the HADS to evaluate their protocols' effects on anxiety and depression. Group one received acupuncture at points believed to help dyspepsia: Neiguan PC6, Hegu LI4, Neiting St44, Zusanli St36, Taichong Lv3, and Zhongwan CV12. Group two received acupuncture on the same meridians, but on points not specific to dyspepsia: Jianshi PC5, Sanjian LI3, Xiangyu St43, Dubi St35, Xingjian Lv2, and Jianli CV11. Acupuncture was administered three times per week over four weeks (12 treatments total). After four weeks, group one experienced significantly greater reduction in dyspepsia, anxiety, and depression compared to group 2.

Haddad-Rodriguez et al (14) studied the effect of auricular acupuncture to ease anxiety in lactating mothers of pre-term infants. 29 subjects were split into two groups: true and sham acupuncture. True group received retention needles unilaterally at: Ear Shenmen, tension, muscle relaxation, anxiety points 1 and 2. Sham group had a simulated needling sensation at the same points, but no needle penetrated the skin and a dull point was kept in place by adhesive tape. Both groups were treated once weekly; and the true and sham needles were kept in place from one treatment to the next. Subjects received between two and 12 sessions. The STAI was used to assess anxiety at baseline and after the course of treatment. Salivary cortisol levels were also collected and analyzed as a secondary measure. The authors found that this protocol did not produce a significant change in anxiety. They also found that the salivary cortisol levels did not correlate with STAI scores.

Bao et al (15) examined the effect of acupuncture on post-menopausal women with breast cancer taking aromatase inhibitors that cause muscular symptoms as a side-effect. They looked at a number of quality-of-life factors including sleep, hot flashes, and anxiety as measured by the HADS. They split 47 subjects into a Real Acupuncture (RA) group and a Sham Acupuncture (SA) group. RA group received acupuncture at Guanyuan CV4, Qihai CV6, Zhongwan CV12, Hegu LI4, Neiguan PC6, Taixi Kd3, Zusanli St36, Yanglingqian GB34, and Shugu UB65. SA received non-penetrating, retractable needles at 14 non-acupuncture points. Both groups were treated once weekly for 20 minutes. Data was collected at baseline, and after four and eight weeks of treatment. RA was more effective in treating hot flashes and other menopausal symptoms than SA, but neither protocol was effective in treating anxiety or depression.

Couilliot et al (16) studied acupuncture for relief of chronic pain in geriatric patients living in a care facility. 60 patients received individualized acupuncture, using between five and 11 needles, for eight sessions over 6 weeks. The needles were retained for 10 minutes. After two sessions, 32% of participants reported a subjective lowering of anxiety. But as this drop in anxiety was not quantified, there was no control group, and the points were not standardized, this study does not help guide practitioners in treatment. This was a pilot study though, and their main focus was whether or not the acupuncture would be desired by the patient population. They found that it was.

Kasymjanova et al (17) examined acupuncture's effect on quality of life in patients with lung cancer using the Edmonton Symptom Assessment System (ESAS). 33 subjects received acupuncture twice weekly at Hegu LI4, Neiguan PC6, Taichong Lv3, Sanyinjiao Sp6, Zusanli St36; and at the auricular points: Shenmen, subcortex, and point zero. Deqi was obtained and the needles were retained for 30 minutes. Subjects had between four to 26 weeks of treatment. ESAS was administered at baseline and at the end of the course of treatment. Comparing baseline to the end of treatment, improvements were found in: Nausea, appetite, pain, nervousness, and well-being. The authors pointed out that the lack of control group limited the conclusions that can be drawn from this one-sample study.

Stenor-Victorin et al (18) examined the effect of acupuncture on depression and anxiety on women with poly-cystic ovarian syndrome (PCOS). The women filled out a variety of questionnaires at baseline, after 16 weeks of treatment, and 16 weeks after completion of treatment. Anxiety was measured with the Brief Scale for Anxiety (BSA). 72 women were divided into Acupuncture, Exercise, and Control groups. Women in the acupuncture group received 14 treatments over 16 weeks. The points used were Zhongji CV3, Qihai CV6, Guilai ST 29, Sanyinjiao Sp 6, and Yinlingquan Sp 9 with EA at 2hz; and Hegu LI4 and Neiguan PC6 with manual stimulation every 10 minutes. The exercise group was instructed to perform aerobic exercise for at least 30 minutes, three times per week. Control group was advised that exercise could help, but were given no specific instructions to exercise. Women in the Control and Exercise groups did not meet personally with researchers after the initial contact. After 16 weeks, there were no differences in BSA scores between groups or within groups. At the 32-week follow-up, Acupuncture group had lower BSA score than the Exercise group but not than Control. This protocol does not appear to be especially effective in treating anxiety in this population.

Bastos et al (19) investigated patients with fibromyalgia. The primary focus was pain, but secondary measures were quality of life. 8 women were treated once weekly for two months with acupuncture at Ashi points on the occiput, trapezius, upper chest, and lateral epicondyle. The Beck Anxiety Inventory (BAI) was administered at baseline and at the end of treatment. BAI scores were significantly lower after the treatment, and patients tolerance to pressure at the ashi points was greater. But again there was no control group, so it is unclear how much of this effect was due to the needling.

Anxiety is often treated with antidepressants which can cause sexual dysfunction. Khamba et al (20) examined the effect of acupuncture on this side-effect in 35 subjects,

but they also investigated anxiety and depression. Subjects who were receiving treatment for anxiety received weekly, 15-minute acupuncture with tonifying method at Taixi Kd3, Mingmen GV4, and Shenshu UB23; and Shenmen Ht7 and Neiguan PC6 with even method. Subjects completed the BAI, BDI, and two sexual function questionnaires weekly. The researchers found after 12 weeks that this protocol improved anxiety, depression, and sexual function scores for males but not for females. This study lacked a control group.

Zhou et al (21) published a report comparing acupuncture on all 12 meridians with clonazepam for reducing anxiety in patients diagnosed with generalized anxiety disorder. Unfortunately only the abstract was available. They split 80 patients with anxiety into an acupuncture or medication group. Anxiety was measured with HAMA and brain waves. Subjects were treated over six weeks. The acupuncture protocol included points such as Hegu LI4, Lieque Lu7, Shenmen Ht7, but the other points were not specified in the abstract. After six weeks, HAMA scores were lower in the acupuncture group than the medication group. Brain waves were improved in both groups, with Alpha waves increased and Theta waves decreased. The improvement in brain waves was similar between both groups. Their conclusion was that acupuncture was as effective as medication at calming brain waves and more effective than medication at improving subjects' subjective experience of anxiety.

Deng et al (22) worked with patients suffering chronic fatigue after chemotherapy. Their primary focus was fatigue, but they also looked at anxiety via the HADS. They split 98 subjects into true and sham acupuncture groups and treated them weekly for six weeks. True group received acupuncture at Taixi Kd3, Qihai CV6, Guanyuan CV4, Zusanli St36, Sanyinjiao Sp6, Quchi LI11, Yinxi Ht6; and deqi was obtained. Sham acupuncture group had retractable, blunt needles placed slightly away from the same acupuncture points. Both protocols were found ineffective for treating both the fatigue and anxiety.

Acar et al (23) examined the effectiveness of a press-needle at Yintang Ex-HN-3 for pre-operative anxiety. 52 subjects received a press-needle at either Yintang Ex-HN-3 or at a non-acupuncture point lateral to the eyebrow for 20 minutes pre-surgically. Anxiety was measured with the STAI and a Bispectral Index (BIS) electrode and monitor. After treatment, the Yintang group's STAI state anxiety score and BIS level were lower than baseline but the state anxiety and BIS of the sham group's were not.

(Insert Table 1)

Conclusions:

There are many limitations in many of the studies reported here. Firstly, many studies lack an appropriate control group. Lundeberg et al demonstrated that sham acupuncture is not inert and should not be considered a valid placebo (4). No-treatment groups are also not appropriate controls. Finniss et al have shown that extra verbal and physical contact can establish a placebo effect and affect outcomes (24). If one group is receiving attention once (or more) weekly and the other group is waiting at home, then any benefits may be due to the extra attention and not to the intervention that we are studying. For

this reason, care should be taken to standardize the amount of physical and verbal contact with subjects between groups.

A second problem in many of these studies is the lack of standardization of points used. Research studies must be reproducible and this is not possible when practitioners are allowed to use their own judgment in selecting points. A good study is not evaluating the ability of “acupuncture” to do anything specific- it is evaluating the ability of a particular point protocol. For this reason, the points used and the number of treatments should be consistent between all members of a treatment arm.

The third problem is that some of these point protocols reported in this study should not be expected to reduce anxiety. If a researcher is going to add an anxiety measure to his or her study, there should be reason to assume that the point protocol used will have an impact on anxiety.

There is ever more evidence that acupuncture is effective for many types of anxiety in many different populations. Research should continue to carefully investigate this area of study.

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Table 1: Table one- summary of studies for OA Acupuncture.d

Table one: Summary of studies

Author	Population	Intervention	Control	Measures	Outcome
Carvalho et al (3)	26 women with pmdd	Pc6, Lv3, Gb34, LI4, TW5, Sp5. twice weekly over 8 weeks of	Sham: Brief shallow insertion slightly away from real points	HAM-A	59% drop in anxiety vs. 21% drop in sham.
Reshef et al (5)	20 patients with schizophrenia	8 weeks of individualized treatment	None	STAI, HAM-A	Reduction in anxiety
McPhearson and McGraw (6)	37 military personnel	6 weeks of weekly Ht7, St36, Yintang, Kd3, Lv3, CV4, CV6, Sp6, LI4 plus many other CAM therapies	None	DASS-21, GAD-7	Reduction in anxiety, depression and use of anxiolytic medication
Lu and Lu (7)	108 subjects with history dental/medical anxiety and inability to be hypnotized	Compared one treatment of LI4, Ht7, PC6, or Yintang	Historical control	Ability to be hypnotized, pulse, BP, blood oxygenation	Yintang most effective for hypnosis, LI4 most effective for muscle relaxation, Ht7 best for pulse reduction
Wang et al (8)	48 patients with depression	24 weeks of weekly treatment atGV20, Sishencong, PC6, and EA at Yintang and PC6	Compared to paroxetine	SAS	Reduction in anxiety similar between both groups
Smith et al (9)	26 inpatients with anorexia nervosa	LI4, PC6, GB34, Lv3, St36 and individualized points, 9 treatments over 6 weeks	Compared to acupressure at same points	DAS	No reduction in or between groups
Zhao et al (10)	Rats in ETOH withdrawal	3 one-minute treatments at Ht7 or PC6, or non-acupoint sham	Non-addicted rats, non-acupoint	EPM behavior, Plasma CORT, CRF in amygdala	Ht7 moderates biochemical and behavioral expression or ETOH withdrawal, PC6 and sham point do not.
Bussell (11)	90 healthy undergraduate students	One 20-minute tx at Sishencong, Yintang, Du24, PC6, Ht7, Kd3	Same verbal and physical contact, no needle insertion	STAI	State anxiety lower in acupuncture group
Arvidsdotter et al (12)	120 psychiatric patients	8 weeks of treatment at GV20, CV6, PC6, Ht7, LI4, Lv3, Sp6, St36, and	Conventional treatment arm, Integrative tx arm that included	HADS	Acupuncture and Integrative arms had less anxiety than

		ashi points	acupuncture and psychotherapy		Conventional
Lima Ferreria and Pace (13)	30 subjects with dyspepsia	PC6, LI4, St44, St36, Lv3, CV12 3x/week over 4 weeks	Compared to same frequency of acupuncture at PC5, LI3, ST43, St35, Lv2, CV11	HADS	Group one (correct acupuncture points) had less anxiety
Haddad-Rodriguez et al (14)	29 Lactating mothers of pre-term infants	Auricular Shenmen, tension, muscle relaxation, and anxiety 1&2, treated weekly with retention needles	Sham: Simulated, non-penetrating acupressure	STAI and salivary cortisol level	Both groups reduced anxiety, but no difference between groups
Bao et al (15)	47 Post-menopausal women with breast cancer taking aromatase inhibitors experiencing muscular symptoms	Weekly tx at CV4, CV6, CV12, LI4, PC6, Kd3, St36, GB34, UB65	Sham: Non-penetrating needles at 14 non-acupuncture points	HADS	Neither protocol effective in reducing anxiety
Couilliot et al (16)	60 geriatric patients in assisted living	Individualized treatments, 8 sessions over 6 weeks	None	Subjective report of less anxiety	32% of subjects reported less anxiety
Kasymjanova et al (17)	33 lung cancer patients	Twice weekly tx at LI4, PC6, Lv3, Sp6, St36, Ear: Shenmen, Subcortex, Point Zero. Treated between 4-26 weeks	None	ESAS	Improvements in nervousness and well being
Stenor-Victorin et al (18)	72 women with PCOS	PC6, LI4, and EA at CV3, CV6, St29, Sp6, Sp9 weekly for 16 weeks	Exercise group, no intervention group	BSA	No difference between groups after 16 weeks, no difference between acupuncture and no-treatment group at 32-week follow-up
Bastos et al (19)	8 women with fibromyalgia	Weekly tx for two months at ashi points on occiput, trapezius, upper chest, and lateral epicondyle.	None	BAI	BAI scores lower at end of treatment

Khamba et al (20)	35 patients with sexual dysfunction secondary to antidepressant meds	Weekly tx at Kd3, GV4, UB23, Ht7 PC6 for 12 weeks	None	BAI	BAI improved for males but not for females
Zhou et al (21)	80 patients with generalized anxiety disorder	6 weeks of treatment with acupuncture on 12 meridians (points not specified)	Anti-anxiety medication	HAMA, brain waves	Bai improved more in acupuncture group, both groups improved in brain waves
Deng et al (22)	98 subjects with chronic fatigue after chemotherapy	Kd3, CV6, CV4, St36, Sp6, LI11, Ht6	Sham: Non-penetrating, retractable needles slightly off the same points	HADS	Protocol no effective
Acar et al (23)	52 subjects with pre-operative anxiety	Press-needle at Yintang	Sham: Press-needle at non-acupoint	STAI and BIS	Improvement in STAI and BIS in Yintang group but not in sham