

Contents lists available at ScienceDirect

# Complementary Therapies in Clinical Practice

journal homepage: www.elsevier.com/locate/ctcp



# Acupuncture and electroacupuncture for anxiety disorders: A systematic review of the clinical research



Diogo Amorim <sup>a, \*</sup>, José Amado <sup>b</sup>, Irma Brito <sup>b</sup>, Sónia M. Fiuza <sup>a</sup>, Nicole Amorim <sup>a</sup>, Cristina Costeira <sup>c</sup>, Jorge Machado <sup>d</sup>

- a Instituto de Medicina Integrativa, Rua Afonso Duarte nº10 A, 3030-402 Coimbra, Portugal
- <sup>b</sup> Escola Superior de Enfermagem de Coimbra, Avenida Bissaya Barreto (Polo A), Apartado 7001, 3046-851 Coimbra, Portugal
- <sup>c</sup> Instituto Português de Oncologia de Coimbra, Av. Bissaya Barreto 98, 3000-075 Coimbra, Portugal
- d Instituto de Cièncias Biomédicas Abel Salazar, Universidade do Porto, Rua de Jorge Viterbo Ferreira 228, 4050-313 Porto, Portugal

#### ARTICLE INFO

## Article history: Received 27 January 2018 Accepted 29 January 2018

Keywords: Acupuncture Electroacupuncture Anxiety disorders Anxiety Systematic review

#### ABSTRACT

Anxiety disorders are one of the most common mental health concerns with a major contribution to the global burden of disease. When not treated, anxiety can be aggravated to more serious and complicated health problems. Pharmacology and psychotherapy stand for the conventional treatment for anxiety disorders but these present limited efficacy, especially in the case of chronic anxiety, with high relapse rates and often causing adverse side effects. Clinical research studies render acupuncture as a valid treatment therapy for anxiety disorders without significant adverse effects.

The objective of this paper is to review the literature on the effectiveness of acupuncture and electroacupuncture for the treatment of patients with anxiety disorders in order to find strong scientific evidence for its regular practice in Western culture.

The systematic review of the clinical research was focused on published clinical trials (controlled, randomized and non-randomized) regarding the treatment of anxiety with acupuncture. Only clinical trials where anxiety was treated as the therapeutic target, and not as a secondary measurement or being associated with other health condition or disease, were considered. Two authors extracted the data independently and exclusion and inclusion criteria were set. The search rendered 1135 papers addressing anxiety as a primary therapeutic target. After review, 13 papers were identified to match exclusion and inclusion criteria and were selected for this analysis. Methodology, design, and quality of the research were highly variable and are discussed and compared.

Overall, there is good scientific evidence encouraging acupuncture therapy to treat anxiety disorders as it yields effective outcomes, with fewer side effects than conventional treatment. More research in this area is however needed.

© 2018 Elsevier Ltd. All rights reserved.

## Contents

1.	Introd	luction	. 32				
		Material and methods					
	2.1.	Literature search and inclusion criteria	32				
3.	Resul	ts	. 33				
	3.1.	Acupuncture or electroacupuncture for anxiety treatment	33				
		Type of acupuncture and main acupoints selected					
	3.3.	Control groups	33				
	3.4.	Type on inventories for the assessment of anxiety	35				
	3.5.	Biological measurements of anxiety	35				

E-mail address: administracao@medicinaintegrativa.pt (D. Amorim).

<sup>\*</sup> Corresponding author.

4.	Discussion	. 36
5.	Conclusions	. 36
	Funding	. 37
	Author disclosure statement	
	References	37

#### 1. Introduction

Anxiety disorders are one of the most common mental health concerns. These disorders represent a significant public health problem and are frequently associated with complications and disability. Anxiety has been detected early in life in children within the 5–9 year range, spanning until a 55–59 year range, after which the most common mental health problem becomes depression (GBD 2015) [1].

In fact, depression and anxiety have been reported to contribute substantially to the Global Burden of Disease as stated in the 2015 report (GBD 2015) [1]. Anxiety ranks in the top ten causes of disability worldwide and is the most prevalent psychiatric condition in the European Union (EU) with over 60 million people being affected by this condition [2]. When untreated, anxiety implies significant personal and societal costs due to frequent primary and acute care visits, decreased productivity at work, unemployment and impaired social relationships. In addition, anxiety presents itself as a risk factor for the development of other anxiety-related disorders [2]. While anxiety disorders were previously related to Western countries, new evidence has recently shown that it is, in fact, a worldwide concern [3]. Anxiety is considered a deleterious mood disturbance characterized by persistent feelings of apprehension, despair, tension, and distress with developing physical symptoms such as tachycardia, nervousness and inability to relax. This condition tends to become chronic and interferes with daily life predisposing to other serious health conditions and to engage in an unhealthy lifestyle behavior [4,5]. The terminology "Anxiety disorders" are a general term comprehending several conditions such as panic disorder, social anxiety disorders, separation anxiety disorders, phobias, selective mutism, anxiety induced by substance use, anxiety associated with a medical condition, and generalized anxiety disorder [6]. Pharmacotherapy and psychotherapy are the conventional treatments for anxiety with the former being considered the standard treatment and with the latter being insufficient when used alone in most cases. Regarding pharmacotherapy, anxiolytics, antidepressants or monoamine oxidase inhibitors are used, with benzodiazepines being the most used pharmacological resource as anxiolytics [7]. Nonetheless, pharmacotherapy is not free from concern since they can lead to habituation (especially in long-term treatments), and present side effects and drug interactions, among other problems [8,9]. Due to its chronicity, high relapse rates, and the need for a long-term maintenance treatment, there is an urgent need for an effective treatment of anxiety, with less undesirable side effects. In the last years, non-conventional therapies such as acupuncture are becoming more popular to treat this health problem. Several studies have proved acupuncture as a safe therapy with rare adverse side effects [10,11]. Acupuncture is an ancient energybased traditional Chinese medicine technique, popular in the East but still recent in Western countries. The technique aims at redirecting and harmonizing energy flow along 14 main energy channels called meridians. The technique consists of stimulating with fine needles selected points in the skin within the 360 points that were identified - acupoints. Each internal organ is linked to a specific meridian and the stimulation of a specific acupoint is believed to interact with the corresponding internal organ harmonizing the energy flow [12]. In the view of traditional Chinese medicine, anxiety is mainly a result of an impairment of the heart and kidneys vital energy flow (and lack of communication between them) and a hyperactivity of liver Yang (active and heating force). Acupuncture, by the stimulation of specific trigger points, could, therefore, improve and alleviate this condition [13].

The objective of this literature review is to summarize clinical research regarding acupuncture in anxiety in the last 10 years to prove the efficacy and consistency of this technique in the treatment of this disorder. Acupuncture has rather recently branched into laser acupuncture and electroacupuncture. This review will only focus on acupuncture (A: body (BA) and auricular (AA)) and electroacupuncture (EA).

#### 2. Material and methods

#### 2.1. Literature search and inclusion criteria

A systematic search was performed on the months of July to September of 2017 (Fig. 1) on relevant electronic databases (B-On, PubMed, Scielo, Science Direct and Scopus) and included both the broad term 'anxiety [all fields]' AND 'Acupuncture [all fields]' OR 'Electroacupuncture' [all fields]. Results were limited to 'human' studies published from 2007 to 2017. Only peer-reviewed Englishlanguage publications were considered. Titles and abstracts were scanned to identify papers containing relevant data. This web search yielded 1135 publications from which literature reviews, case studies, opinion or comment papers, and papers focused on general surveys were excluded from analysis.

Repeated papers common to different databases, denied access to full text, papers concerning anxiety and acupuncture but not correlating both, or papers treating anxiety as a secondary effect while treating other conditions, were excluded. The remaining 96 full-text papers were analyzed for eligibility criteria. Studies that did not use A and EA to treat anxiety as a primary target were not considered.

Whenever another health condition was associated with anxiety (such as pain) other acupuncture points were introduced and stimulated in the treatment and therefore, the results regarding the decrease of anxiety could be indirectly related to the stimulation of other acupoints (anxiety unrelated points). Moreover, the reduction of anxiety could also be indirectly related to an improvement of the condition per se, for example, the reduction of pain. Laser acupuncture and acupressure studies were excluded from this review as well. Uncontrolled, prospective, case studies or trials considering a very small group of subjects were also not considered. One paper was excluded because the same authors presented a similar but more complete study 2 months after the submission of the previous work [15]. All studies had to use an established rating scale or other effective measures to access the degree of anxiety. Although only clinical trials are reviewed, other types of publications were read to identify relevant studies such as review papers. After the exclusion and inclusion criteria accordingly to the method

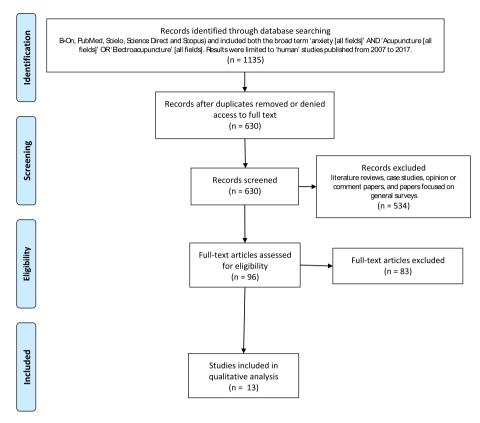


Fig. 1. PRISM diagram showing the number of studies included and excluded from the systematic review. Scheme adapted from Moher et al. [14].

[14] presented in Fig. 1, 13 papers were selected for the present review and are listed in Table 1.

# 3. Results

# 3.1. Acupuncture or electroacupuncture for anxiety treatment

All 13 studies reported an anxiety decrease for their treatment group relative to the control groups. These results were consistent across clinical studies from different countries and cultures. Of the 13 papers selected, only one paper regarding electroacupuncture (EA) and anxiety was elected [16]. In fact, most of the papers found using EA keywords concerned animal studies or were study protocols. One other trial was found but was excluded due to the lack of confidence of the results as TENS sham acupuncture was used on acupuncture points and the number of sessions of the treatment groups varied [17]. Only the trial of Wu and Liu [16] was considered in this review. Their research shows that both EA group and the control/pharmacotherapy group presented a high success rate (>80%) on the ability to decrease anxiety. However, only the control group presented several side effects in contrary to EA, which presented none. More investigation in this area is needed, with high quality results and more consistent methods for the sake of research on the field. For instance, during the analysis of other EA papers, excluded for their lack of quality, it was verified that the frequency of the current was not homogenous or even similar across trials. The methods used were in fact very diverse across studies. Although EA studies are still scarce regarding this subject, it seems to be an interesting technique to pursue, especially in the case of chronic or more complex cases of anxiety disorders.

# 3.2. Type of acupuncture and main acupoints selected

Eight trials concerned body acupuncture [9,18-24], four trials, auricular acupuncture [25–28] and one electroacupuncture [16]. Regarding auricular acupuncture, Karst [25] and Michalek-Sauberer [27], used the same 3 acupoints (relaxation, tranquilizer and master cerebral), Shayestehfar [28] used 2 acupoints (relaxation and shenmen) but Klausenitz [26] used more points, namely, lung, shenmen, kidney, subcortex and adrenal gland. In all cases, auricular acupuncture was effective in reducing anxiety. Regarding body acupuncture, the most used points were PC6 (Neiguan) (used by 7 [9,16,19–22,24] trials), EX-HN3 (Yintang) (used by 6 [16,18–20,22,23] trials) and HT7 (Shenmen) (used by 5 [16,20-22,24] trials). PC6 was common to all BA trials that used multiple acupoints. Two trials used one single point, in that case, both used Yintang point (EX-HN3) [18,23].

# 3.3. Control groups

Of the 13 papers, two [9,27] used no intervention at all on the control group, three submitted their control group to pharmacological treatment [16,19,24], two used Sham acupuncture [18,22], two used a waiting list control group [21,28] and three [20,23,26] submitted their control groups to the same situational environment, with Bussell [20] being quite thorough having control patients' acupoints swabbed with alcohol and ensuring the same level of physical and verbal contact. One study used two control groups: a no intervention control group, and a placebo group [25]. A sum of different control groups or waiting list control group may be the most ethical and adequate option, as well as having different control groups if this option is available for the research team. Sham

**Table 1**Summary of the studies included in the review.

Study	Intervention	Diagnosis	Design	Points Used	Control	Outcome	Results
Arranz et al., 2007 (Spain) Pubmed	BA = 34 C = 20 30 min	BAI	10 sessions 1 year Anxious women 30-60 years	SI3, HT3, HT5, PC6, LI4, LI11, TE5, CV3, CV4, CV6, CV15, GB34, GB43, ST36, SP6, LR2, BL60, KI6, GV20	No intervention	BAI Chemotaxis Phagocytosis Lymphoproliferation NK activity Superoxide anion levels	BA significantly improved immune functions relative to the values presented before treatment, with parameters approaching the ones of healthy individuals (Control). There were immune parameters that augmented and some that diminished, revealing not only a regulatory effect of acupuncture on the immune system but also a modulatory one.
Karst at al. 2007 (Germany) Pubmed	AA = 19 Placebo = 19 D = 19 C = 10 25 min	VAS STAI-X1 STAI-X2 Sedation score Heart rate Oxygen saturation	1 session: situational anxiety Patients having dental extractions Randomized controlled trial	AA: relaxation, tranquilizer, and master cerebral points (external ear/ nondominant side) Placebo: finger and liver points with blunt needle	Control: No intervention Drug group: 4 mg midazolam	VAS STAI-X1 STAI-X2 Heart rate Oxygen saturation	There were no visual differences on oxygen saturation for any group. Heart rate was equal for all groups except for the no treatment group which presented an increased rate. Both auricular acupuncture $(p=0.012)$ and intranasal midazolam $(p<0.001)$ have an anxiety reducing effect relative to the control group, however, the duration of the sedation was longer for the midazolam group.
Yuan et al., 2007 (China) Pubmed	$BA = 29 \\ D = 29 \\ BA + D = 28 \\ 45 min$	CCMD-3-R HAM-A	36 sessions 6 weeks hospital patients having never received any anxiolytic agent or psychoactive drug HAMA ≥ 15 18-65 years	Main points: Sishenzhen and Dingshenzhen. PC6, HT7, SP6 bilaterally Depending on patient were also used: LR3, ST36 OR LR3, LR14, RN17, ST40 OR BL15, ST36 OR LR2, PC8	20 mg fluoxetine or paroxetine + 0.4–1.6 mg alprazolam per day if necessary	Clinical global impression (CGI) scale Plasma levels of ACTH and CS Platelet content of 5- HT	The efficacy of the three schemes was not significantly different $(p > 0.05)$ being all equivalent in alleviating patients' anxiety. ACTH and 5-HT levels decreased in all groups $(p < 0.05)$ . Changes on CS level were not significative for any group test. Acupuncture scored best for less side effects $(p < 0.01)$ and, more importantly, prevented them in the combined treatment $(acupuncture + drug)$
Wu and Liu 2008 (China) B-on	EA = 34 D = 33 80-100 Hz 30 min	HAM-A	30 sessions Once a day Post-stroke anxious patients	GV20, GV24, EX-HN3, GV26, LI4, LR3, HT7, PC6		НАМА	Both EA and D group were efficient on relieving anxiety with a success rate over $80\%$ (p < 0.01). No differences were found between both groups (p > 0.05) but EA did not present side effects.
Michalek- Sauberer et al., 2012 (Austria) B-on	AA = 61 SA = 60 C = 61 20  min	VAS STAI-X1 STAI-X2	1 session: situational anxiety Adult patients (≥18 years old) scheduled for elective dental procedure with VAS score ≥ 3 Prospective, randomized, sham-controlled, single-blinded	AA: Relaxation point, tranquilizer point, master cerebral point SA: Finger, shoulder and tonsil AA points		STAI-X1	hot present stude effects. Auricular acupuncture reduced anxiety ( $p < 0.001$ ) more effectively than Sham acupuncture ( $p < 0.001$ ) by 3.6 points before the dental treatment. In contrast, in the control group anxiety increased significantly before the dental treatment (10 points above AAG) ( $p = 0.004$ ). No significant differences were found between different dental treatments ( $p = 0.188$ ) or in gender ( $p = 0.198$ ).
Isoyama et al., 2012 (Brazil) Pubmed	BA = 22 SA = 21 25 min	НАМ-А	4 weeks 4-6 sessions Woman undergoing in vitro fertilization (<45 years old) Prospective, randomized single-blinded	BA: HT7, PC6, CV17, GV20 and EX-HN3 SA: outside accupoints	Sham acupuncture	нам-а	(p=0.198). HAM-A score was significantly lower in the BA group than in the SA group (p=0.0008). It was verified a 19.4% decrease in anxiety for the SA group and of 34.9% for the BA group.
Acar et al., 2013 (Turkey) Pubmed	BA = 26 SA = 26 20 min	BIS electrode STAI	controlled study 1 session: situational anxiety Adult patients (18 -65 years old) Prospective, randomized single-blinded controlled study	Yintang (EX-HN3)	Sham acupuncture	BIS electrode STAI	BIS values in BA were significantly lower than in SA ( $p < 0.0042$ ). BIS values for BA ( $p < 0.0004$ ), but not SA group, were lower than the baseline values. The STAI-S values decreased in BA ( $p = 0.018$ ) but not in SA ( $p = 0.156$ ) group.

Table 1 (continued)

Study	Intervention	Diagnosis	Design	Points Used	Control	Outcome	Results
Bussell 2013 (USA) Pubmed	BA = 44 C = 46 20 min	STAI-Y1 STAI-Y2	1 session, situational anxiety Undergraduate university students (18–30 years old) Randomized, single-blind study	EX-HN1, GV24, EX- HN3, HT7, PC6, KI3	Laid in table for 20 min. Accupoints were touched and swabbed with alcohol. There was the same physical and verbal contact.	STAI-Y1	The BA group presented reduced state anxiety ( $p=0.0146$ ) and improved memory, immediately after treatment ( $p=0.0134$ ). The memory improvement, however, was not shown to be correlated to reduced anxiety.
Errington- Evans 2015 (UK) Pubmed	BA1 = 25 BA2/C = 15 30 min	STAI	10-12 weeks 10 sessions randomized controlled trial	PC6, HT7, LR3 bilaterally	Waiting list control group receiving acupuncture later in time (BA2)	STAI	There was a significant improvement in state and trait anxiety in BA1 relative to the control waiting list/control group (BA2) (p < 0.0001). BA2 showed similar significant improvements after receiving acupuncture. Improvement were maintained after 10 weeks of follow-up for both groups.
Attias et al., 2016 (Israel) Pubmed	$\begin{array}{l} D/C = 60 \\ CDRGI + D = 60 \\ BA + D = 60 \\ GI + D = 60 \\ R + D = 60 \\ GI + R + D = 60 \\ 30\text{-}60  \text{min} \end{array}$	VAS	1 session, situational anxiety randomized controlled trial	PC6, KI3, LR3, EX- HN3	Drug/control: 10 mg Oxazepam OR 5-10 mg Diazepam 120–160 min before going to holding room	VAS	All complementary and alternative medicine treatments were effective on reducing anxiety (p < 0.001). The treatments did not differ between each other in efficacy in contrast with the results for the drug group with no effectiveness on reducing anxiety.
Klausenitz et al., 2016 (Germany) Pubmed	AA = 12 SA = 13 C = 15 Needles left 1 day 'New pyonex' needles	VAS STAI		MA-IC1 (Lung), MA- TF1 (Shenmen), MA- SC (Kidney), MA-AT1 (Subcortex) and MA- TG (Adrenal gland) Bilaterally	0	VAS STAI	AA was effective on reducing state anxiety relative to the control group $(p = 0.003)$ , and more effective than SA group $(p = 0.021)$ before the exam. Nonetheless, both interventions were effective on reducing anxiety on the students relative to the control group.
Shayestehfar et al., 2016 (Iran) Pubmed		CSAI-2 Heart rate Skin conductance	Male football players (16–18 years old) Randomized, controlled trial	Relaxation point, Shenmen point	Control patients were put on a waiting list		BA group showed significant decrease on cognitive and somatic anxiety compared to the SA group $(p=0.001)$ and to the C group on a waiting list $(p<0.001)$ . The BA group $(p=0.004)$ also presented decreased heart rate relative to the SA group.
Wiles et al., 2017 (UK) B-on	BA = 57 C = 49 30 min	STAI-S6 APAIS	Neurosurgical patients ≥ 16 years old Randomized, controlled trial	EX-HN3	Seated for 30 min	STAI-S6 APAIS	There was a significative reduction of anxiety ( $14\%-30\%$ reduction) in BA (p < 0.001) relative to the C group (p = 0.829). No adverse effects were verified.

C: Control; BA: Body Acupuncture; D: drugs; AA: auricular acupuncture; SA: Sham acupuncture; BAI: Beck Anxiety Inventory; CDRGI: Compact Disk Recording of Guided Imagery; GI: individual Guided Imagery; R: reflexology; CCMD-3-R: Chinese classification scheme and diagnostic standard for psychotic diseases; VAS: visual analogue scale; STAI: Spielberg State Trait Anxiety Inventory, STAI-X1, STAI-Y1 or STAI-S measures state anxiety and STAI-X2, STAI-Y2 or STAI-T measures trait (baseline) anxiety; STAI-6: sixitem short form of the stai-trait anxiety Inventory; HAM-A: Hamilton Anxiety Scale; BIS: diposable bispectral index electrode; CSAI-2: Competitive State Anxiety Inventory-2; CS: Corticosteroid; ACTH: Adrenocorticotrophic Hormone; 5-HT: 5-hydroxytryptamine; APAIS: Amsterdam Pre-operative Anxiety and Information Scale.

acupuncture is still a controversial control group as it is known not to be innocuous and still ambiguous on to what extent it is possible to compare between studies.

# 3.4. Type on inventories for the assessment of anxiety

Different types of inventories were used by the selected trials, among them, four used VAS [19,25–27], three used HAM-A [16,22,24], one used BAI [9], seven used STAI [18,20,21,23,25–27], one used CCMD-3-R [24], one used CSAI-2 [28], and one APAIS [23]. Although BAI inventory seems to be the strictest inventory, being able to distinguish between anxiety and depression, STAI inventory is the most popular inventory to determine the degree of anxiety among the clinical trials.

# 3.5. Biological measurements of anxiety

Acupuncture is recognized by World Health Organization [29] as

a viable treatment for several medical conditions. However, in the Western countries, it has been cautiously recommended. One of the main reasons for this suspiciousness is in part due to the scarce scientific or measurable evidence validating its benefits.

To thrive in the Western countries, acupuncture effects need to be translated and validated quantitatively, not only through inventories but also by the measurement of biological parameters. A few studies addressing biological quantification of acupuncture effects have been reported. Of the studies considered in this review, two of them considered biochemical parameters to measure anxiety. Since acupuncture acts upon the nervous system, it can interact and modulate several systems in the body, including the immune system [30–33].

Arranz and coworkers [9] screened the variation of several immune functions which are described to be good health markers and known to be impaired in emotional distress situations. The study shows that chemotaxis, phagocytosis, lymphoproliferation and NK activity are significantly improved by acupuncture. Patients with

abnormally high levels of superoxide anion and lymphoproliferation had these parameters significantly diminished after treatment. Overall, acupuncture brought the immune parameters closer to the control levels of healthy untreated woman. More importantly, besides the proven stimulatory effect of acupuncture, it was also verified to present a modulatory effect of the immune system augmenting or diminishing the levels of the immune parameters as needed to achieve the healthy parameters. Although this is a preliminary study without placebo-controlled studies, it presents interesting results that should be further pursued [9].

The biochemical mechanism for anxiety seems to be related to a neurotransmitter (5- hydroxytryptamine (5-HT) hyperfunction) and neuroendocrine function disorder (excessive excretion of adrenocorticotropic hormone (ACTH), corticosteroid (CS) and prolactin) [24,34]. In the semi-randomized controlled clinical research of Yuan and coworkers [24], plasma CS and ACTH and platelet 5-HT levels were measured in patients to attest the efficacy of acupuncture relative to a control group administered with common pharmacological treatment and further compared to a group receiving combined therapy (acupuncture + pharmacology). The main findings of the study were that all groups treated anxiety effectively, however, not only did acupuncture have fewer side effects, but it also aided the prevention of the side effects of the drugs on the combined therapy group. It would be interesting to expand the study to a larger group of patients and most importantly, to use the same acupuncture points for all patients to validate these results. Three other studies [18,25,28] complemented their results with the measurement of physiological parameters. Karst et al. [25] used heart rate and oxygen saturation measurements. Acar et al. [18] used a bispectral index electrode and Shayestehfar et al. [28] heart rate and skin conductance. Although Karst [25] team did not find any alteration relative to the oxygen saturation level, they observed a decreased heart rate for all treatment groups compared to the control group. Shayestehfar et al. [28] describes a decreased rate of heartbeat for the body acupuncture group relative to the sham acupuncture one. Furthermore, this study also measures skin conductivity and correlates skin sweat to the somatic manifestation of anxiety. They found a significant decrease in anxiety (p = 0.001) compared to both sham and control groups (p < 0.001). Finally, Acar et al. [18] uses a bispectral index (BIS) electrode to monitor the patients. Usually, EEG is used to assess cerebral functions, namely, central nervous system physiologic alterations, disease, or the effect of drugs on the brain. Due to the complexity of the EEG signal, BIS technique has revealed to be a good alternative to measure cortical electrical activity. Higher values for BIS implicate caution and care. On their study, Acar et al. found out that BIS values decrease significantly in relation to the sham acupuncture group (p < 0.0042) and in comparison to baseline levels (p < 0.0004).

# 4. Discussion

The interest of researchers in the treatment of anxiety disorders using acupuncture is a worldwide trend, as observed by the country of origin of the selected studies for this review. This trend is supported by several factors such as growing knowledge on the anatomophysiologic mechanism of action of acupuncture, an empirical validation of acupuncture's benefits and results, and the growing interest of the general public regarding this therapy. Recent studies stress the safety of acupuncture with no evidence of significative side effects which renders it a very useful tool [35–37].

From the literature research and the analysis on the selected papers, limitations to the method were encountered such as method heterogenicity, inadequate diagnosis, and poor experimental design. The lack of homogeneity of the results is not only due to the absence of a standard protocol or guideline to treat

anxiety but also to the uncertainty when distinguishing between anxiety and depression by using inadequate diagnosis methods/inventories. Also, there are different schools of acupuncture (China, Japan, Korea, India) with theory varying from diagnosis to acupoints allocation. This fact also brings difficulties when aiming at the parametrization of the technique.

As extensively discussed before, clinical studies using Sham acupuncture found that this type of control also leads to the decrease of anxiety, however, this decrease was generally to a lower extent than the one verified for real acupuncture. Nevertheless, the use of Sham acupuncture has been discussed as to be its reliability as a control group.

During the screening of research papers for this review, we found quite some research which did not have a control group whatsoever or were confronted with a wide variety of different types of control groups. We understand the difficulties that arise when choosing a control group, sometimes determined by external or logistic factors rather than a poor experiment planning, however, it is difficult to compare results when different control groups are used.

As a result of our research, if we would have to advance with a treatment proposition for the research acupuncture treatment of anxiety, we would suggest that the following points should be always included in an anxiety treatment design: PC6, EX-HN3 and HT7 for body acupuncture and relaxation, tranquilizer and master cerebral points for auricular acupuncture. The BAI inventory would be also one of our preferable choices due to the ability to distinguish between anxiety and depression, together with the use of biological markers for the assessment of anxiety levels. Our choice of a control group would be the waiting list control group.

Finally, we are aware of some limitations of this review. The fact that it is restricted to reports in English is a limitation as there are certainly valuable works published in other languages. Furthermore, this systematic review was dedicated not only to acupuncture but also to electroacupuncture, and only 1 paper on this subject is presented. This is due, not only to the low amount of papers published in this area but also due to the low quality of the reports which were therefore not included. We hope to see more work published in this area in the future.

#### 5. Conclusions

The information gathered in this systematic review leads to a first observation and conclusion that is that different methodologies (different acupoints, design, duration, type of acupuncture) lead to similar results which are decreased levels of anxiety. This fact urges for more research in this area to attest if the results are indeed a result of acupuncture therapy. For this purpose, parametrization of a method seems to be of paramount importance. The call for parametrization perhaps demands more acupuncture focused on research purposes only, rather than having studies compiling clinical cases of patients that seek clinical treatment on their own. On another hand, as much as a parametrization of the method seems necessary, we understand that acupuncture treats the patient as a whole, and depending on the cause or somatic complaints of a patient, different treatment strategies could be chosen.

The currently available treatment options for anxiety present limited efficacy, toxicity, drug interactions and risk of drug addiction. Acupuncture seems to be an adequate, safe and effective alternative for the treatment of anxiety. More research studies in this area are however required with more robust methodologies to ensure acupuncture efficacy on the treatment of anxiety disorders. Electroacupuncture studies are scarce in the literature regarding this subject and research in this field could be very useful.

Furthermore, the review was intended to focus primarily on anxiety non-related to any other health condition and therefore, a few acute/situational anxiety clinical research studies were included in this review, such as the case of preoperative patients. Although these results are quite important, care must be made not to extrapolate their result/effectiveness to chronic anxiety cases.

In sum, there seems to be promising results that justify for more planned research in this area, not only based on self-report or clinical assessment but also using other types of measurements.

# **Funding**

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

#### **Author disclosure statement**

No competing financial interests exist.

# References

- T. Vos, et al., Global, regional, and national burden of neurological disorders during 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015, Lancet Neurol. 388 (2016) 1545–1602.
- [2] O. Remes, C. Brayne, R. Van der Linde, L. Lafortune, A systematic review of reviews on the prevalence of anxiety disorders in adult populations, Brain. Behav. 6 (7) (2016), e00497.
- [3] A.J. Baxter, K.M. Scott, T. Vos, H.A. Whiteford, Global prevalence of anxiety disorders: a systematic review and meta regression, Psychol. Med. 43 (5) (2013) 897–910.
- [4] D.P. Sniezek, I.J. Siddiqui, Acupuncture for treating anxiety and depression in women: a clinical systematic review, Med. Acupunct. 25 (3) (2013) 164–172.
- [5] A.T. Beck, N. Epstein, G. Brown, R.A. Steer, An inventory for measuring clinical anxiety: psychometric properties, J. Consult. Clin. Psychol. 56 (6) (1988) 893–897.
- [6] A.P. Association, Diagnostic and Statistical Manual of Mental Disorders: DSM-5, fifth ed., American Psychiatric Association, Arlington, VA, 2013.
- [7] B. Bandelow, L. Sher, R. Bunevicius, E. Hollander, S. Kasper, J. Zohar, H.-J. Moller, Guidelines for the pharmacological treatment of anxiety disorders, obsessive – compulsive disorder and posttraumatic stress disorderin primary care, Int. J. Psychiatr. Clin. Pract. 16 (2012) 77–84.
- [8] S. Goyatá, C. Avelino, S. Santos, J.D. Souza, M. Gurgel, F. Terra, Effects from acupuncture in treating anxiety: integrative review, Rev. Bras. Enferm. [Internet] 69 (3) (2016) 564–571.
- [9] L. Arranz, N. Guayerbas, L. Siboni, M. De la Fuente, Effect of acupuncture treatment on the immune function impairment found in anxious women, Am. J. Chin. Med. 35 (1) (2007) 35–51.
- [10] A. White, A cumulative review of the range and incidence of significant adverse events associated with acupuncture, Acupunct. Med. 22 (3) (2004) 122–133.
- [11] C.M. Witt, D. Pach, B. Brinkhaus, K. Wruck, B. Tag, S. Mank, S.N. Willich, Safety of acupuncture: results of a prospective observational study with 229,230 patients and introduction of a medical information and consent form, Forsch Komplementmed 16 (2009) 91–97.
- [12] R. Liebowitz, L. Smith, The Duke Encyclopedia of New Medicine: Conventional and Alternative Medicine for All Ages, Rodale Books, 2006.
- [13] N. Samuels, C. Gropp, S.R. Singer, M. Oberbaum, Acupuncture for psychiatric illness: a literature review, Behav. Med. 34 (2) (2008) 55–64.
- [14] D. Moher, A. Liberati, J. Tetzlaff, D.G. Altman, Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement, PLoS Med. 6 (6) (2009), e1000097.
- [15] S. Zarei, M. Shayestehfar, A.-H. Memari, T. Seif-Barghi, V. Sobhani, Acupuncture decreases competitive anxiety prior to a competition in young athletes: a randomized controlled trial pilot study, J. Compl. Integr. Med. 2016 (2016).

- 20150085.
- [16] P. Wu, S. Liu, Clinical observation on post-stroke Anxiety neurosis treated by acupuncture, J. Tradit. Chin. Med. 28 (3) (2008) 186–188.
- [17] M. Dias, G.C. Vellarde, B. Olej, Effects of electroacupuncture on stress-related symptoms in medical students: a randomised placebo-controlled study, Acupunct. Med. 32 (2014) 4–11.
- [18] H. Acar, O. Cuvaş, A. Ceyhan, B. Dikmen, Acupuncture on Yintang point decreases preoperative anxiety, J. Alternative Compl. Med. 19 (5) (2013) 420–424
- [19] S. Attias, B.L. Keinan, Z. Arnon, E. Ben-Arye, A. Bar'am, G. Sroka, I. Matter, M. Somri, E. Schiff, Effectiveness of integrating individualized and generic complementary medicine treatments with standard care versus standard care alone for reducing preoperative anxiety, J. Clin. Anesth. 29 (2016) 54–64.
- [20] J. Bussell, The effect of acupuncture on working memory and anxiety, J. Acupunct, Meridian Stud. 6 (5) (2013) 241–246.
- [21] N. Errington-Evans, Randomised controlled trial on the use of acupuncture in adults with chronic, non-responding anxiety symptoms, Acupunct. Med. 0 (2015) 1–5.
- [22] D. Isoyama, E. Cordts, A.M. de Souza van Niewegen, W. de Almeida Pereira de Carvalho, S.T. Matsumura, C.P. Barbosa, Effect of acupuncture on symptoms of anxiety in women undergoing in vitro fertilisation: a prospective randomised controlled study, Acupunct. Med. 30 (2012) 85–88.
- [23] M.D. Wiles, J. Mamdani, M. Pullman, J.C. Andrzejowski, A randomised controlled trial examining the effect of acupuncture at the EX-HN3 (Vintang) point on pre-operative anxiety levels in neurosurgical patients, Anaesthesia 72 (3) (2017) 335—342.
- [24] Q. Yuan, J.-n. Li, B. Liu, Z.-f. Wu, R. Jin, Effect of jin-3-needling therapy on plasma corticosteroid, adrenocorticotrophic hormone and platelet 5-HT levels in patients with generalized anxiety disorder, Chin. J. Integr. Med. 13 (4) (2007) 264–268.
- [25] M. Karst, M. Winterhalter, S. Münte, B. Francki, A. Hondronikos, A. Eckardt, L. Hoy, H. Buhck, M. Bernateck, M. Fink, Auricular acupuncture for dental anxiety: a randomized controlled trial, Anesth. Analg. 104 (2) (2007) 295–300.
- [26] C. Klausenitz, H. Hacker, T. Hesse, T. Kohlmann, K. Endlich, K. Hahnenkamp, T. Usichenko, Auricular acupuncture for exam anxiety in medical students—a randomized crossover investigation, PLoS One 11 (12) (2016), e0168338.
- [27] A. Michalek-Sauberer, E. Gusenleitner, A. Gleiss, G. Tepper, E. Deusch, Auricular acupuncture effectively reduces state anxiety before dental treatment—a randomised controlled trial, Clin. Oral Invest. 16 (2012) 1517–1522.
- [28] M. Shayestehfar, T. Seif-Barghi, S. Zarei, A. Mehran, Acupuncture Anxiolytic Effects on Physiological and Psychological Assessments for a Clinical Trial, Scientifica, Cairo, 2016, 4016952.
- [29] W.H. Organization, Acupuncture: Review and Analysis of Reports on Controlled Clinical Trials, World Health Organization, 2002.
- [30] H.O. Jin, K.Y. Zhou, K.Y. Lee, T.M. Chang, W.Y. Chey, Inhibition of acid secretion by electrical acupuncture is mediated via β-endorphin and somatostatin, Am. J. Physiol. 271 (1996) G524–G530.
- [31] K.B. Koh, The relationship between stress and natural killer-cell activity in medical college students, Jpn. J. Psychosom. Med. 3 (1993) 3–10.
- [32] K. Nishijo, H. Mori, K. Yosikawa, K. Yazawa, Decreased heart rate by acupuncture stimulation in humans via facilitation of cardiac vagal activity and suppression of cardiac sympathetic nerve, Neurosci. Lett. 227 (3) (1997) 165-168.
- [33] Q.-W. Xie, Endocrinological basis of acupuncture, Am. J. Chin. Med. 9 (4) (1981) 298.
- [34] G. Gerra, A. Zaimovic, U. Zambelli, M. Timpano, N. Reali, S. Bernasconi, F. Brambilla, Neuroendrocrine responses to psychological stress in adolescents with anxiety disorder, Neuropsychobiology 42 (82–85) (2000) 82.
- [35] Y.J. Jeong, Y.S. Park, H.J. Kwon, I.H. Shin, J.G. Bong, S.H. Park, Acupuncture for the treatment of hot flashes in patients with breast cancer receiving antiestrogen therapy: a pilot study in Korean women, J. Alternative Compl. Med. 19 (8) (2013) 690–696.
- [36] J. Weiss, S. Quante, F. Xue, R. Muche, M. Reuss-Borst, Effectiveness and acceptance of acupuncture in patients with chronic low back pain: results of a prospective, randomized, controlled trial, J. Alternative Compl. Med. 19 (12) (2013) 935–941.
- [37] M.J. Mallory, K.A. Croghan, N.P. Sandhu, V. Lemaine, A.C. Degnim, B.A. Bauer, S.S. Cha, I.T. Croghan, Acupuncture in the postoperative setting for breast cancer patients: a feasibility study, Am. J. Chin. Med. 43 (1) (2015) 45–56.