

SOUTH BAYLO UNIVERSITY

Efficacy of Acupuncture in Treating Depression
—A Review of Evidences

By

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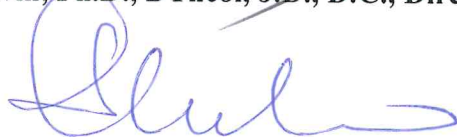
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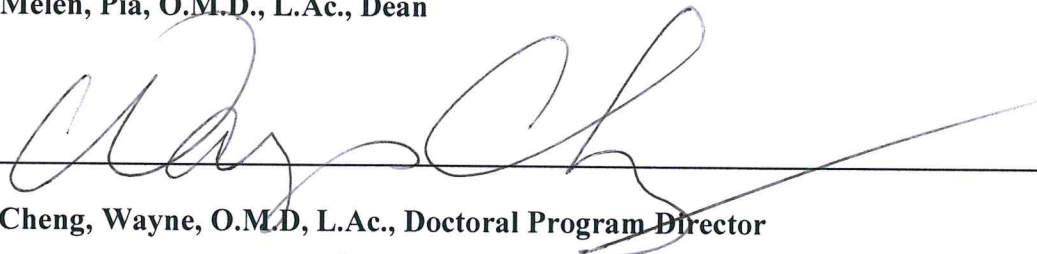
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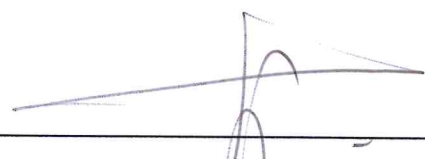
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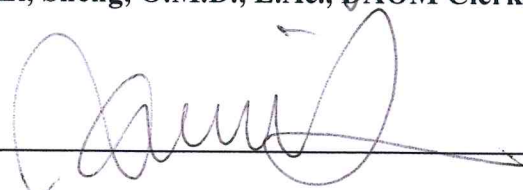
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Efficacy of Acupuncture in Treating Depression
- A Review of Evidences

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South Baylo University at Anaheim, 2016

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ABSTRACT

The main task of this literature review is to find evidence of the effectiveness of acupuncture in treating depression, a common syndrome in the modern society. In this overview, the available systematic reviews and trial reports related to evaluation of acupuncture for the management of depression, and to identify the safety of acupuncture in treatment of depression were collected and studied in this review.

The data and reports of studies were searched in EBSCO host, Medline, Alt Health Watch, and PubMedPubMed with full text for the time period from 2004 to 2016 (01/2004 to 06/2016).

The key words “acupuncture” and “depression” were entered into EBSCO Medline, PubMedPubMed and 12 articles on the effect of acupuncture on depression were selected for comparison and analysis.

According to the literature the most common used points for treatment of depression were Yin Tang, LI4, ST36, ST40, SP6, KD3, and LV3, HT7, DU20. These points were utilized to balance the disorder between qi and blood, and among organs in the body. They also unblock the stagnation of qi and blood, and regulate the flow of qi and blood in the channel and collateral.

Key-words: acupuncture, depression

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I. INTRODUCTION

1. Outline

Depression is a major problem in the world today. Unipolar major depression accounts for 4.4% of the world's total burden of the disease as measured by Disability Adjusted Life Years¹.

Depression is a serious psychiatric illness that involves symptoms such as depressed or sad mood, loss of interest or pleasure in activities, changes in weight, difficulty sleeping or oversleeping, energy loss, feeling of worthlessness, psychomotor changes, and thoughts of death or suicide.

Depression includes major depressive disorder (MDD), minor depression (MinD), antenatal depression, postpartum depression (PPD), childhood depression, geriatric depression, organic depression, vascular depression, drug-induced depression, post-stroke depression (PSD), and depression comorbid with other diseases. MDD is common and can be disabling. Point prevalence rates of MDD are estimated at 5% to 13% for women and 2% to 8% for men, with an estimated lifetime prevalence of 16.2% and a 12-month prevalence of 6.6%. ***Over 80% of people who died by suicide are clinically depressed in the months prior to their deaths².***

Depression is the second most common mental health disorder after anxiety. About 30% of people who visit a primary care practitioner have symptoms of depression. However, only some of these people have major depression. People who become depressed typically do so in their mid-teens, 20s, 30s, although depression can begin at almost any age, including during childhood. People born in the latter part of the 20th century seem to have higher rate of depression and suicide than those of the previous generations, in part because the rate of substance abuse have increased.

An episode of depression, if untreated, typically lasts about six months but sometimes may last for 2 years or more. Episodes tend to recur several times over a lifetime.

According to a national survey in the UK reported by Hopton et al, psychological problems are the third most common reason for patients to seek acupuncture after musculoskeletal and neurological conditions³. According to an earlier UK survey of general practitioners (GPs), respondents identified depression as an area where there is an 'effectiveness gap' in primary care; depression was identified as the second most problematic condition to treat after musculoskeletal conditions⁴. Moreover, depression is a growing problem which is set to become the second leading cause of disease burden worldwide by 2020, according to the Global Burden of Disease Study⁴. So it is highly concerning that up to 60% of patients do not respond adequately to pharmacological antidepressant treatment and 30% do not adhere to medication. Patients have expressed the view that there is an overreliance on prescribed antidepressant medication and they are keen to have a range of possible treatment choices. The net result is that an interest in non-pharmacological options is growing⁴.

By choosing to live entirely within the modern world we are therefore choosing lives of decreased interaction with the earth, lives which have great potential for stagnation.

If our external environment can be maintained on a fairly stable level, our bodies do not need to use their capacities for adaptation. As these capacities atrophy we begin to desire an environment which challenges us less and less until stagnation becomes preferable to the pain of adaptation.

Depression is merely one of the many symptoms of stagnation and the imbalances which result from stagnation. Opening up the pathways of interactions, freeing stagnation and restoring the dynamic balance are the primary objects of the acupuncture treatment of depression⁵.

2. Definition

According to American psychological Association, depression is defined as:

A fluctuation in normal mood ranging from unhappiness and discontent to an extreme feeling of sadness, pessimism, and despondency⁶.

In psychiatry, it is any of the depressive disorder or any mood disorder that typically have sadness as one of their symptoms, such as dysthymic disorder and major depressive disorder⁶.

3. Causes

The exact cause of depression is unclear, a number of factors may make depression more likely. They include a family tendency (heredity), side effects of certain drugs, and emotionally distressing events. Particularly a loss of close relatives. Depression does not reflect a weakness of character and may not reflect a personality disorder, childhood trauma, or poor parenting. Depression may arise or be worse without any apparent or significant life stresses.

Genetic abnormalities may contribute to disease. They can affect the function of substances that help nerve cells communicate (neurotransmitters): dopamine, norepinephrine, serotonin are neurotransmitters that may be involved in depression¹⁷.

Table 1: Some causes of Depression⁷

Condition	Examples
Brain and nervous system disorders	Brain tumors, Dementia (in early stages), Head injury, Multiple sclerosis, Parkinson's disease, Sleep apnea, Stroke, Seizures that affect the temporal lobe (complex partial seizures)
Cancers	Abdominal cancers (ovary or colon), Cancer spreading throughout the body (metastatic), Cancer of the pancreas
Connective tissue disorders	Systemic lupus erythematosus (Lupus)
Hormonal disorders	Addison's disease, Cushing's disease, Diabetes, High levels of parathyroid hormone, low and high levels of thyroid hormone, Low levels of pituitary hormones (hypopituitarism)
Infections	AIDS, Influenza, Mononucleosis, Syphilis (late stage), Tuberculosis, Viral hepatitis, Viral pneumonia
Nutrition disorder	Pellagra (vitamin B6 deficiency), Pernicious anemia (vitamin B12 deficiency)
Drugs	Alcohol, Amphetamine withdrawal, Amphotericin B, Antipsychotic drugs, Beta-blockers (some), Cimetidine, Contraceptives

	(oral), Corticosteroids, Cycloserine, Hormone (estrogen) therapy, Interferon, Mercury, Methyldopa, Metoclopramide, reserpine, Thallium, Vinblastine, Vincristine
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4. Diagnostic Criteria for depression:

A. Five or (more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.

- Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad, empty, hopelessness). (Note: In the children and adolescents, can be irritable mood.)
- Markedly diminished interest or pleasure in all, or almost all activities most of the day, nearly every day (as indicated by either subjective account or observation).
- Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month) or decrease or increase in appetite nearly every day. (Note: in children, consider failure to make expected weight gain.)
- Insomnia or hypersomnia nearly every day.
- Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being showed down).
- Fatigue or loss of energy nearly every day.
- Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).

- Diminished ability to think or concentrate, or decisiveness, nearly every day (either subjective account or as observed by others).

- Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

B. The symptoms that cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

C. The episode is not attributable to the physiological effects of a substance or to another medical condition.

Note: Criteria A-C represent a major depressive episode.

Note: Responses to a significant loss (e.g., bereavement, financial ruin, losses from a natural disaster, a serious medical illness or disability) may include the feelings of intense sadness, rumination about the loss, insomnia, poor appetite, and weight loss noted in criterion A, which may resemble a depressive episode. Although such symptoms may be understandable or considered appropriate to the loss, the presence of a major depressive episode in addition to the normal response to a significant loss should also be carefully considered. This decision inevitably requires the exercise of clinical judgment based on the individual's history and the cultural norms for the expression of distress in the context of loss.

D. The occurrence of the major depressive episode is not better explained by schizoaffective disorder, schizophrenia, schizophreniform disorder, delusional disorder, or order specified and unspecified schizophrenia spectrum and other psychotic disorders.

E. There have never been a manic episode or a hypomanic episode.

Note: This exclusion does not apply if all of the manic-like or hypomanic-like episodes are substance-induced or are attributable to the physiological effects of another medical condition⁸.

5. The treatment of depression in conventional Western medicine:

Psychotherapy

Psychotherapy is sometimes called "talking therapy." It is used to treat mild and moderate forms of depression. A licensed mental health professional helps people with depression focus on behaviors, emotions, and ideas that contribute to depression. They also help the depressed person identify and understand life problems that contribute to their illness in order to enable them to regain a sense of control. Psychotherapy can be done on an individual or group basis and can include family members and spouses. It is most often the first line of treatment for depression.

Medicines

Medicines are commonly used to treat depression. The cost of medicines and potential side effects are important considerations when choosing this type of treatment for depression.

Some common antidepressants:

SSRIs

Selective serotonin reuptake inhibitors (SSRIs) are common medications. They fight depression symptoms by decreasing serotonin blockers in the brain. They're the most commonly prescribed class of antidepressants. They come in the form of:

- sertraline (Zoloft)

- fluoxetine (Prozac)
- citalopram (Celexa)
- escitalopram (Lexapro)
- paroxetine (Paxil, Pexeva)
- fluvoxamine (Luvox)
- trazodone (Oleptro)

SSRIs help most patients with depression, but they also cause side effects. Sexual side effects are among the most common in these antidepressants.

SNRIs

Serotonin and norepinephrine reuptake inhibitors (SNRIs) help improve serotonin and norepinephrine levels in the brain. Options include:

- desvenlafaxine (Pristiq)
- duloxetine (Cymbalta)
- venlafaxine (Effexor XR)

Desvenlafaxine and venlafaxine are similar in terms of efficacy. Duloxetine offers the added benefit of pain relief in addition to treating depression.

TCA's

Tricyclic antidepressants (TCAs) are often prescribed when SSRIs or other antidepressants don't work. TCAs can cause constipation, dry mouth, and fatigue. More serious side effects include low blood pressure, irregular heart rate, and seizures. TCAs are available as:

- amitriptyline

- amoxapine
- clomipramine (Anafranil)
- desipramine (Norpramin)
- doxepin
- imipramine (Tofranil)
- nortriptyline (Pamelor)
- protriptyline (Vivactil)
- trimipramine (Surmontil)

Tetracyclic Antidepressant

One tetracyclic antidepressant, maprotiline, is used for depression and anxiety.

Dopamine Reuptake Blocker

Bupropion (Wellbutrin) is a mild dopamine and norepinephrine reuptake blocker, used for depression, seasonal affective disorder (SAD) and also smoking cessation.

5-HT₂ Receptor Antagonists

Two 5-HT₂ receptor antagonists, nefazodone and trazodone, are used to treat depression.

5-HT₃ Receptor Antagonists

One 5-HT₃ receptor antagonist, vortioxetine (Brintellix), is used to treat depression.

MAOIs

Monoamine oxidase inhibitors (MAOIs) are older drugs that treat depression by preventing the breakdown of norepinephrine, dopamine, and serotonin. They're more difficult for patients to take than most other antidepressants because they interact with many prescription drugs,

nonprescription drugs, and foods. They have many adverse effects and can't be combined with other antidepressants or stimulants.

MAOIs are rarely a doctor's first choice of drug to prescribe.

MAOIs include:

- isocarboxazid (Marplan)
- phenelzine (Nardil)
- selegiline (Emsam), a transdermal patch
- tranylcypromine (Parnate)

Noradrenergic Antagonist

Mirtazapine (Remeron) is used primarily for depression.

Table 2: Cost of antipsychotics for treatment-resistant depression⁹

Generic name	Brand name	Average monthly cost
Aripiprazole tablet	Abilify	\$636 - \$939
Asenapine tablet	Saphris	\$758 - \$761
Clozapine tablet	Clozaril	\$219 - \$568

Clozapine tablet	Generic	\$77 - \$356
Iloperidone tablet	Fanapt	\$701 - \$749
Combination capsule with olanzapine plus fluoxetine	Symbyax (Zyprexa plus Prozac)	\$402 - \$742
Olanzapine tablet	Zyprexa	\$423 - \$1,242
Olanzapine dissolvable tablet	Zyprexa Zydis	\$500 - \$1,441
Paliperidone tablet	Invega	\$590 - \$881
Quetiapine tablet	Seroquel	\$272 - \$1,197
Quetiapine tablet	Seroquel XR	\$182 - \$549
Risperidone tablet	Risperdal	\$186 - \$535
Risperidone tablet	Generic	\$68 - \$233
Ziprasidone capsule	Geodon	\$575 - \$669

Other Medications

Other depression medications don't fall into the typical classes. These are called atypical antidepressants. Depending on condition, your doctor may prescribe one of these alternatives instead.

Electroconvulsive therapy

Electroconvulsive therapy (ECT) is a procedure in which of an electric current is used to produce a seizure in the patient. It is believed that ECT results in the release of chemicals in the brain that aid communication between nerves. It is used for severe forms of depression and is rarely used in patients with epilepsy¹⁰.

Alternative treatments

Alternative treatments can sometimes provide relief that traditional western medicine cannot. While some alternative treatments have become accepted as part of modern health care practice, others still have not been proven safe and effective.

Whether they are scientifically effective, alternative therapies—by providing forms of relaxation and relief from stress—have a place in healing and general health and well-being. Examples of alternative therapies include acupuncture, guided imagery, chiropractic treatments, yoga, hypnosis, biofeedback, aromatherapy, relaxation, herbal remedies, massage, and many others.

In general, alternative therapies by themselves are effective for mild, but not more severe forms of depression.

Hormone replacement therapy (HRT) in women

Depression is more common in women than in men. Changes in mood with premenstrual syndrome (PMS) and premenstrual dysphoric disorder (PMDD), after childbirth, and following menopause are all linked with sudden drops in hormone levels.

Hormone replacement is a treatment currently used to relieve symptoms of menopause such as night sweats and hot flashes. By using HRT, women can help prevent osteoporosis and possibly reduce memory loss. There are many advantages to using HRT for relieving symptoms of menopause; and although they may, in the future, be found to help depression in some women, these hormones can actually contribute to depression. Be sure to tell your doctor if you have had depression before and are considering HRT.

6. Depression in TCM

In the book “Chinese Internal Medicine (中医内科学),” by Zhang, depression disease is described as Yu Zheng (郁症):

Depression refers to dysfunction of viscera due to emotional unease and qi stagnation. It is manifested as depressive temper, restless emotion, distending pain in hypochondria, easy upset easy cry, blocking sensation in the throat, insomnia, and every kind of complex symptoms¹¹.

In “The Psyche in Chinese medicine” by Giovanni, the correspondence between Chinese mental emotional conditions and depression in Western medicine was described as follows:

The complex of symptoms that we call “depression” in the West corresponds not to one but to at least five main categories of mental-emotional disturbances in classic (four of them were chosen to describe to depression in the review because their manifestations like the symptoms of depression disease. Xin Ji Zheng Chong is more similar to anxiety, so it is not appropriate to study in this topic).

Yu Zheng 郁证: Depression

Chinese term for depression is Yu¹² 郁.

Bai He Bing 百合病: Liliun syndrome

The Liliun syndrome is described in the Essential Prescriptions of the Golden Chest (Jin Gui Yao Lue) as following:

The patient wants to eat, but reluctant to swallow food and unwilling to speak. He or she wants to lie in bed but cannot lie quietly as he or she is restless. He or she wants to walk but is soon tired. Now and then he or she may enjoy eating but cannot tolerate the smell of food. He or she feels cold or hot but without fever or chills, bitter taste or dark urine. No drugs are able to cure this syndrome. After taking the medicine the patient may vomit or have diarrhea. The disease haunts the patient and, although he or she looks normal, he or she suffering. The pulse is rapid¹².

Mei He Qi 梅核气: Plum-pit syndrome (Globus Hystericus)

Mai He Qi was first described in Jin Gui Yao Lue. This book says:

The patient has a suffocating feeling as if there was a piece of roast meat stuck in the throat. Use Ban Xia Hou Po Tang¹².

Zang Zao 脏燥: Agitation

Zang zao is also described in Jin Gui Yao Lue.

The patient is suffers from Agitation (Zang zao), feels sad and tends to weep constantly as if she were haunted. She stretches frequently and yawn repeatedly. The decoction of Fu Xiao Mai, Gan Cao and Da Zao can calm the patient¹².

The pathology of depression in Chinese medicine is considered as Yu (郁). Yu has the double meaning of “depression” and “stagnation”¹².

Yu as mental depression

Besides meaning “stagnation”, Yu also means “mental depression”. Some Chinese doctors say that, in a broad sense, Yu indicates stagnation and it is the pathological basis for very many disease; in a narrow sense, Yu refers to the disease category of “mental depression”¹².

Patterns and treatments of depression in TCM:

Depression is a disease caused by visceral dysfunction and emotional unease. With the passing of time, it will consume Heart Qi, Ying and Blood lead to restless temper, organic disharmonize. Depression syndrome can be divided to two main patterns. Early stages, they mostly belong to excessive syndrome, do not use tonic only use sedated techniques in the treatment; later period, they almost transfer to deficient syndrome, prior nourishing Ying and Blood, invigorating Qi and supporting healthy Qi in the treatment¹¹.

Etiology

The etiology of depression includes the following factors.

- Emotional stress:
 - + Anger
 - + Sadness and grief
 - + Worry
 - + Guilt

- Constitutional traits
- Irregular diet
- Overwork

Nowadays, acupuncture has been used for depression treatment in many countries worldwide. There are numerous scientific studies about the mechanism of action of acupuncture in treating diseases, including depression. These studies show efficacy of acupuncture in treating depression.

According to acupuncture theory, health is a status of dynamic balance between Yin and Yang, Qi and the Blood. If there is blockage or stagnation, excess or deficiency of Yin and Yang or Qi and Blood, the disease will be formed and appeared afterward. If the Qi or Blood imbalance can be corrected, the physical and emotional problem will follow suite. It is for this reason that acupuncture is uniquely suited for the treatment of depression.

Studies have shown that treating depression with acupuncture can have a positive, holistic effect on depressed patients, particularly when acupuncture is combined with psychotherapy and herbs.

Acupuncture is being integrated with Western medicine, particularly for treatment of pain, nausea, asthma, and neurological conditions. Although the exact mechanism for acupuncture treatment is unknown, it is associated with an increase in the level of neuro-biologically active substances, such as endorphins and enkephalin. There are also data indicating that acupuncture induces the release of norepinephrine, serotonin, and dopamine¹³.

Inserting needles into the body's key energy pathways can stimulate the central nervous system, releasing chemicals into the muscles, spinal cord, and brain. This can promote the body's natural

healing abilities by altering brain chemistry and by helping to release neurotransmitters and neuro-hormones.

II. Materials & Methods

The reports of studies were searched in EBSCO host, MEDLINE, Alt Health Watch, and PubMed with full text, from 2004 to 2016 (01/04-06/16). This review is focusing on the role of acupuncture in treatment of depression. The main goal is to find out the effect acupuncture cause on depression patients.

The key-words used for literature search were depression, depression in Western medicine, acupuncture in TCM, and evidences of the effects of acupuncture treatment upon depression.

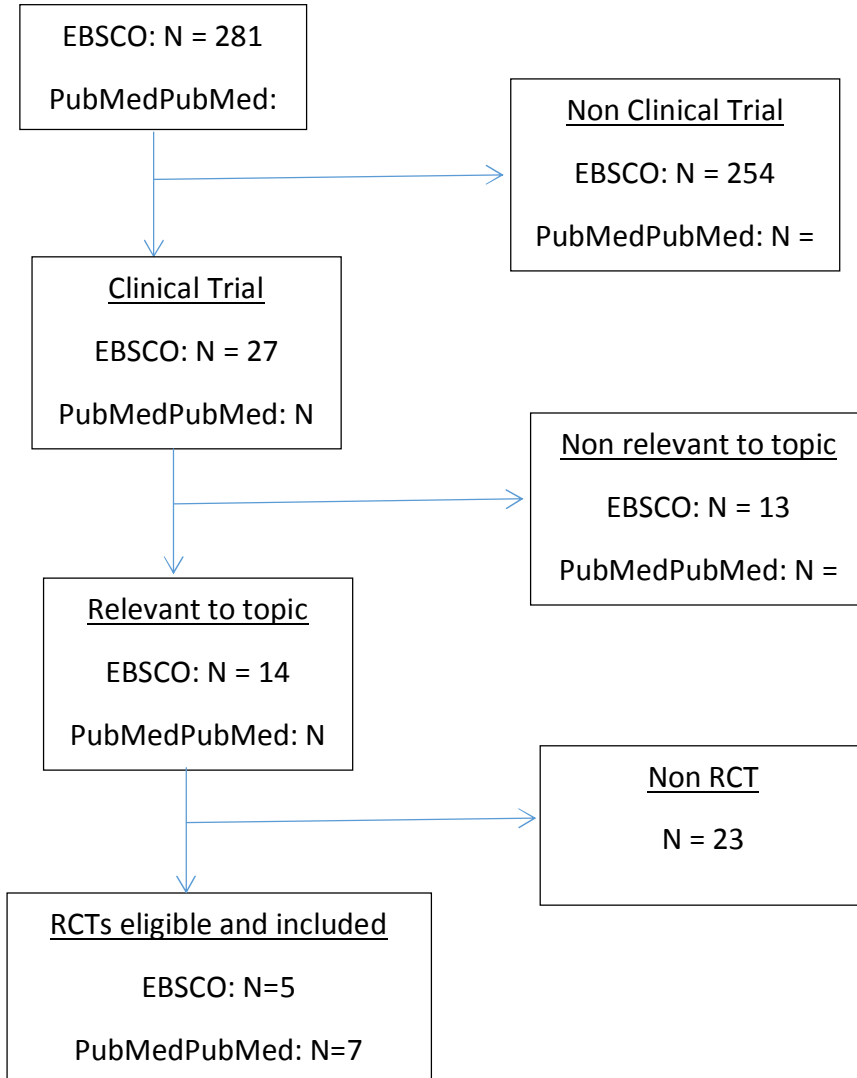
Twelve research papers were collected during the period since 2004 to 2016 (01/04-06/16).

All of them are suitable papers for this review, because they chose acupuncture as the main medical interference for depression treatment and it was human studies only.

The criteria of inclusion and exclusion:

- Inclusion:
 - + Period: 2004-2016 (01/04-06/16)
 - + The research method used: Randomized control trials (RCTs)
 - + The content: focusing on the effects of acupuncture on depression.
- Exclusion:
 - + Papers related to other psychiatric problems such as anxiety alone, or bi-polar alone were excluded.
 - + Paper related to laser acupuncture were excluded. This kind of acupuncture has not been approved in California acupuncture board, yet.
 - + Papers related to animal experiment were excluded.

Figure 1. Research and Selection of Articles Process



III. Results

The phrase “acupuncture and depression” was entered EBSCO research databases and PubMed engine, 496 articles were retrieved, but only 12 studies met the criteria, and they were selected for this review. All of these articles are in English language. They were carried out in China, Hong Kong, England, and United States.

2051 patients were participated in total of 12 studies, these patients met the diagnosis of depression (DSM-IV-TR, Diagnostic and Statistical Manual of Mental Disorders-Text Revision, 4th ed. or Chinese Classification and Diagnostic Criteria of Mental Disorders, 3rd ed. CCMD-3). The sample size of these studies is from 43 to 755.

The outcome were measured by Beck Depression Inventory (BDI), Clinical Global Impression – Severity scale CGI-S, Hamilton Depression Rating Scale (HDRS), Hamilton Rating Scale for Depression (HAM-D), Minnesota Multiphasic Personality Inventory (MMPI), Montgomery-Asberg Depression Rating Scale (MADRS), Patient Health Questionnaire-9 (PHQ-9 scale), and Self-rating Depression Scale (SDS). Results with p-values of 0.05 or less are considered valid.

Statistic numbers and evidences such as clinical characteristics, acupuncture methods, acupuncture types, etc., will be described in tables, figures and flow charts.

Table 3: Characteristics of included studies

Study	Sample size	Research method & outcome measures	Interventions	Results
Fan et al, 2016	n = 163	Randomized, single-blind, placebo-controlled; SF-36	Three-armed design, Ratio: 1:1:1	Acupuncture can effectively improve the quality of life of depressive patient. The scores in SF-36 scale increased significantly.
			One treatment group: Acupuncture, Moxibustion, Intradermal embedding of needle	
			Two control groups: 1. Acu-point shallow stab 2. Non-acupoint shallow stab	
Man et al, 2014	n = 43	Single-blind, randomized controlled trial; HAMD; CGI-S; BDI	Two-armed design, SSRI, EA for both group.	Great reduction of scores on HAMD-17 for DCEAS and n-CEA at week 4: -11.6±2.3 for DCEAS -11.2±1.9 for n-CEA DCEAS could be effective in reducing depressive symptom of stroke patients
			Treatment group (n=23): DCEAS	
			Control group (n=20): Sham DCEAS	
Macpherson et al, 2013	n = 755	Three-arm pragmatic Randomized controlled trial; PHQ-9; BDI	Three-armed design, Ratio: 2:2:1	Improving of 5 - 6 points on the PHQ-9 for both groups
			One treatment group: Acupuncture	
			Two control groups: 1. Counseling 2. Usual care	
Wang et al, 2013	n = 60	Non-blinded randomized controlled trial; MMPI; SDS; MADRS	Two-arm design, Ratio: 1:1	MMPI subscale decreased from 68.80±8.19 to 60.25±11.16 for depression patients in treatment group (P<0.01)
			Treatment group: Electro-acupuncture	
			Control group: Paroxetine	
Sun et al, 2013	n = 75	Prospective Randomized controlled trial;	Three-armed design Ratio: 1:1:1	HDRS scores were lower from baseline to week 6 for three groups. EA-Treatment group:
			Two treatment groups: 1. Electro-acupuncture	

		HDRS	DU20, ST36 2. Fluoxetine	23.80±2.93 to 9.45±3.17 EA-Control group: 22.81±3.25 to 9.94±2.18 Fluoxetine-Treatment group: 23.32±3.49 to 12.12±4.38 After 6 weeks, Serum GDNF significantly increased in all groups compared with baseline, GDNF of EA group: From 20.94±6.82 to 24.79±3.98 (P<0.05)
Zhang et al, 2012	n = 73	Single-blind, randomized, controlled study; HAMD; CGI-S; SDS	Two-armed design, Fluoxetine for both groups Treatment group (n=38): DCEAS Control group (n=35): n-EA	The scores were lower on the scales for both groups: DCEAS at day 21: -8.66/HAMD-17; -0.74/CGI-S; -13.06/SDS n-EA at day 21: -6.27/HAMD-17; -0.74/CGI-S; -8.38/SDS
Andreescu et al, 2011	n = 57	Randomized controlled trial; HDRS	Two-armed design Treatment group (n=28): Electro-acupuncture Control group (n=29): 4 patients removed Sham electro stimulation	The decreases in HDRS from baseline to post intervention: -7.4 for EA group -7.9 for control group (P=0.81)
Manber et al, 2010	n = 150	Randomized controlled trial; HDRS	Three-armed design Treatment group (n=52): Acupuncture special Two control groups: 1. Acu non special (n=49) 2. Massage (n=49)	At week 8, the scores in HRSD-17 were lower for all three groups (about -12 to - 8; Fig. 2-Manber, 2010). (There were not the exact numbers from Fig.2/ Manber, 2010)
Feng et al, 2011	n = 80	Randomized controlled trial; HAMD; SDS	Two-armed design, Ratio: 1:1 Treatment group (n=40): Manual acupuncture Control group (n=40):	The scores before and after treatment of patients: SDS: Treatment group: 64.12±5.34 to 43.64±5.28 Control group:

			Fluoxetine	64.24±4.98 to 50.76±5.42 HAMD: Treatment group: 20.92±2.38 to 9.88±1.27 Control group: 20.72±2.74 to 13.72±2.05
Fu et al, 2009	n = 440	Multi-center randomized controlled trial; SDS	Three-armed design,	SDS before treatment and after 3 months of 3 groups: Acupuncture group: 67.06±12.01 to 43.18±9.38 Prozac group: 67.06±12.01 to 46.99±12.67 Non-acup needling group: 68.45±11.15 to 52.90±12.94
			One treatment group (n=176): Manual acupuncture	
			Two control groups: 1. Prozac (n=176) 2. non acu-point (n=88)	
Duan et al, 2009	n = 95	Randomized controlled trial; HAMD	Two-armed design,	HAMD scores at the baseline and the end point Fluoxetine + Acupuncture 23.8±4.0 to 10.1±5.1 Fluoxetine group: 25.1±3.7 to 12.7±5.5
			Treatment group (n=48): EA + Fluoxetine	
			Control group (n=47): Fluoxetine	
Zhao et al, 2006	n = 60	Randomized controlled trial; HAMD	Two-armed design, Ratio: 1:1	HAMD scores before and after treatment Acupuncture group: 35.36±11.27 to 17.70±4.57 Fluoxetine group: 36.08±11.52 to 18.96±4.61
			Treatment group (n=30): Acupuncture	
			Control group (n=30): Fluoxetine	

Abbreviations: Acu: Acupuncture; EA: Electric Acupuncture; DCEAS: dense cranial electro-acupuncture stimulation; n-CEA: non-invasive cranial electro-acupuncture; n-EA: non-invasive electro-acupuncture

From twelve RCTs in this review, three studies were single-blind RCT^{14,15,16}, five studies were three-armed RCT^{14,17,18,19,20}, seven RCTs were two-armed design^{15,16,21,22,23,24,25}, one study was Pragmatic RCT¹⁸.

In three single-blind designs, acupuncturists knew the grouping of participants, but the participants unable distinguish the difference of grouping to minimize the expected effects. It seems to be impossible to design double-blind for acupuncture clinical trials, because Acupuncturist need to know the acupuncture point's location for inserting into the patients.

In five three-armed studies, a RCT²⁰ had two treatment groups, the rest of them included two control groups inside each study.

The comparisons were made between acupuncture and control group, and between each groups at the baseline and the endpoint of treatment. These comparisons reported the improvement on the outcome measurements.

Among these studies, conventional body acupuncture^{14,17,18,19,23,25}, ear acupuncture^{7,8}, scalp acupuncture¹⁵, electro-acupuncture^{20,21,22,24}, dense cranial electro-acupuncture stimulation (DCEAS)^{15,16}, moxibustion¹⁴, or intradermal embedding needle¹⁴ were contributed to treatment groups, while sham acupuncture^{14,15,16,17,19,21}, massage¹⁶, counseling¹⁸, usual care¹⁸ or antidepressant^{16,17,20, 22, 23,24,25} were used in control groups.

Using the different outcome measurement, almost results of twelve RCTs indicated the great significant reduction of scores before and after treatment on the scales. Five studies demonstrated the lower scores compared the baseline with the endpoint on HAMD^{15,16,22,23,25}, three studies had the decreases on HDRS^{19,20,21}, two studies gained the great improvement on SDS^{17,23}, there was an improving on PHQ-9 of 5-6 points from study of Macpherson et al, the scores of MMPI subscale also decreased for depression patients from 68.80±8.19 to 60.25±11.16 in treatment group (P<0.01), only the score on SF-36 increased significantly from study of Fan et al¹⁴ performed acupuncture can effectively improve the quality of life of depressive patient.

Table 4: Acupuncture used in intervention arms

Study	Acupuncture interventions
Fan et al, 2016	Conventional body acupuncture was applied at LI4, LIV3, DU20, Yintang, 30 min retention; Moxibustion and then intradermal embedded needling (0.35 mm × 25 mm filiform needle) UB15, UB18 (24 sessions/12 weeks)
Man et al, 2014	Electro-acupuncture was applied at LI4-LI11, ST36-LIV3; DCEAS at DU20-Yintang, Shishencong-GB15, GB8, Taiyang, ST8, Electric stimulation with continuous 2 Hz – 9 V waves, lasting 30 min. (12 sessions/4 weeks)
Macpherson et al, 2013	Conventional body acupuncture was depending on Zang Fu diagnosis (38 syndrome were recorded) to select the acupuncture points. The additional therapies were acupressure, moxibustion, electro acupuncture. Most common used syndromes: Liver Qi stagnation, Spleen deficiency, Heart deficiency, Kidney deficiency. Most common used acupuncture points: SP6, LIV3, ST36, LI4, PC6, Yintang, Kid3, Ht7, Du20, LIV8, ST40 Average 10 acupuncture treatments per patient.
Wang et al, 2013	Conventional acupuncture was inserted at DU20, Sishencong, Yintang, PC6, HT7, SP6 with 20 min treatment session, 3 times/week for 24 weeks (72 sessions/24 weeks)
Sun et al, 2013	Electro acupuncture was applied at DU20, ST36 for treatment group, once daily for 30 minutes at a time. 5 times per week (30sessions/6weeks).
Zhang et al, 2012	DCEAS during Fluoxetine Electrical stimulation was delivered on the following 6 matches of forehead acu-points DU20-Yintang, left Shishencong-GB15, right Shishencong-GB15, bilateral GB8, bilateral Taiyang, bilateral ST8, they are innervated by trigeminal nerve for DCEAS. Electrical stimulation with continuous waves 2 Hz, 9 V, constant current for 30 min, 3 times per week for 3 weeks (9 sessions/3weeks)
Andreescu et al, 2011	Electro acupuncture was applied at DU20, Yintang for treatment group; Current of 3-5 mA, frequency of 2 Hz was applied 30 minutes per treatment, 2 treatments per week for 6 weeks (12 sessions/6weeks).
Manber et al, 2010	Acupuncture specific address depression-relevant patterns, according to the principles of Traditional Chinese Medicine and following a published standardized treatment manual. Seven to twelve points were inserted in each treatment. Neutral to moderate needle stimulation until the arrival Qi sensations were obtained. 25 min per treatment, 2 times per week for the first 4 weeks and weekly for 4 more week (12 sessions/8 weeks)
Feng et al, 2011	Patients in treatment group received acupuncture on the acu-points of ST40, SP9, SP10, SP6, Yintang, DU20, Sishencong, PC6, Shenmen (TF4-ear), with

	the method of neutral of supplementation and drainage, 20-30 min per treatment per day for 30 days (30 sessions/30 days).
Fu et al, 2009	Conventional acupuncture on LI4, LIV3, DU20, Yintang, Ear-points (The thumbtack-type needles were intracutaneously embedded in ear points, Liver and Heart, and kept for 3 days). 30 min for needle retention, 2 times/ week for 3 months (24 sessions/12 weeks)
Duan et al, 2009	Electro acupuncture on DU20, Yintang; MA at LI4, LIV3; LIV2, GB43; HT7, PC6; SP6, ST36; or KID3, KID6; frequency of 120-250/min; intensity was set according to the tolerance of patient; 30 minutes for a treatment; a time per day, 6 times per week for 6 weeks (36 session/6 weeks)
Zhao et al, 2006	Conventional acupuncture on Taiyang, DU24, UB4, DU20, PC6, HT7, SP6, LIV3; quick twisting manipulation in small amplitude at a frequency of 200/min for 2 minutes; 30 min needle retention; a treatment per day for 30 days 30 acupuncture treatment per 30 days (30 sessions/30 days)

Acupuncture intervention

Seven studies^{14,17,18,19,23,24,25} used conventional acupuncture for their treatment groups. In these studies, the acupuncture manipulations were carried until the arrival Qi sensations were obtained, the needle retention was about 20-30 minutes for a time.

Five rest studies^{15,16,20,21,22} applied electro-acupuncture for the patients. Especially, two of them used DCEAS in their RCTs. The frequency of 2 Hz were applied in three studies^{15,16,21}, and the frequency of 120-250/min was used for another one²².

DU20 was used in eleven studies except study of Manber¹⁵, the couple DU20 and Yintang appeared in nine RCTs^{14,15,16,17,18,21,22,23,24}. This couple points were becoming the main points of the acupuncture formulas for depression, in this review.

In their RCTs, Man et al and Zhang et al used low frequency (2 Hz, 9 V waves) for DCEAS because it could induce biochemical changes in brain for alleviating depressive symptoms^{15, 25}.

This acupuncture method made the improvement for depression patients.

LIV3, LI4, PC6, HT7, KID 3, ST36, ST 40, SP9, SP6, Sishencong, Taiyang, ear-Shenmen were applied for patients in the studies used conventional acupuncture. These points made the rebalance between Yin and Yang, Qi and Blood, and unblocked the stagnation of Qi and Blood.

The treatment sessions for acupuncture in twelve RCTs were from 9 to 72, and the treatment periods were lasting from 3 weeks to 24 weeks.

In addition, in their study, Sun et al were going to measure the concentration of serum GDNF before and after intervention. They also compared GDNF level with HDRS score to evaluate the correlation between them. After six weeks of treatment, the serum GDNF significantly increased in all three groups. The GDNF level was inversely correlated with HDRS score in both EA treatment group and EA control group (GDNF of EA group after six weeks of treatment, compared with the baseline: From 20.94 ± 6.82 to 24.79 ± 3.98 $P < 0.05$. The HDRS score was lower for EA group after 6 weeks, compared with the baseline: 23.80 ± 2.93 to 9.45 ± 3.17).

Comparator intervention

Six RCTs in this review chose sham acupuncture for their control groups^{14,15,16,17,19,21}. Sham acupuncture were acupuncture shallow stab, non-acupoint shallow stab¹⁴, sham DCEAS^{15,16}, sham electro stimulation²¹, non-acupoint¹⁷, acupuncture non special¹⁹. Five studies^{17,22,23,24,25} selected antidepressant for their comparator arms. Antidepressant were Fluoxetine^{17,22,23,25} (Prozac), Paroxetine²⁴. A study²⁰ chose electro acupuncture, another¹⁸ had counseling and usual care for their control groups. Massage was selected for comparator intervention of Manber¹⁹ study. Almost comparator interventions in the studies gained improvement after treatment included sham groups, and there were not the explanation for this appearance.

Comparisons between acupuncture and comparator intervention

Some RCTs^{19,21,24} demonstrated there were not the significant differences of the effects between treatment group and control group. In the rest of twelve studies in this review, according to the outcome measurements, there were the significant greater improvement of treatment group than control group. Some studies showed the greater reduction of treatment group compared with control group^{1,15,16}. The side effect of acupuncture group made comparison with antidepressant is smaller^{16,17,22,23}.

IV.DISCUSSION

With 12 overview studies above, acupuncture and depression were accessed and studied minutely. Finding the evidences of acupuncture efficacy in depression treatment is the mission of this review.

Depression was diagnosed in both Western medicine and Oriental medicine by the professional Doctors. The researchers often used DMS-4 to diagnose depression in western medicine and some others used CCMD-3 to diagnose depression in TCM.

Many of scales as BDI, MMPI, SDS, MADRS, HDRS and PQ-9 were used to measure the level of depression at the baseline, during the treatment, and at the end of the study.

In these studies, acupuncture was assigned to intervention groups, including manual acupuncture alone, electro-acupuncture alone, combination between conventional acupuncture and electro-acupuncture, acupuncture combined with antidepressant. The control groups or comparisons often were SHAM acupuncture, massage, counseling, usual care or antidepressant.

Most commonly used acupuncture points for patients suffer from depression are DU20, Yintang, SP6; LV3; ST36; LI4; PC6.

With the great appearance of couple point Du20 and Yintang in acupuncture treatment for depression in the difference studies, and with the significant improvement of depression on the outcome measures of this combination beside the other points, the electro-acupuncture of DU20 and Yintang is becoming a popular formula, the popular acupuncture protocol for depression disease.

Auricular points such as Shenmen, Heart point, Liver point also applied in some studies in this review to calm the spirit, relax the emotion to relieve depression.

All of the studies in this review concluded that acupuncture is effective in relieving symptoms of depression. All of results from the studies in this review determined that acupuncture made the great improvement for depression disease, according to the scores on the outcome measurements.

In my own suggestion, the brain MRI right after acupuncture for depression (Ex: doing acupuncture on DU20, Yin Tang, LV3, ST36, and SP6...) will be required. Which neuro transmitters, which hormones are secreted by the treating of these points, the answers should be studying clearly. These studying will give us the more objective and scientific evidences to evaluate the efficacy of acupuncture for depression deeper, clearer.

V. CONCLUSION

It could be concluded that acupuncture has a solid foundation and experience in treating depression with a strong evidence such as:

The decrease of MADRS, SDS score was greater in the treatment group than in the control group²⁴. The increase of scores on SF-36 indicated that acupuncture can effectively improve the quality of life of patients with depression¹⁴.

EA and fluoxetine had similar curative effects on DD patients²⁰.

Using ANCOVA, MacPherson found that there was an improvement of five to six points on the PHQ-9 scale¹⁸, etc.

Furthermore, acupuncture can be combined with antidepressant, augment the effects and reduce the side effects of them²².

More clinical trials with large sample size, longer study, randomized control trials, and finding out the effect of acupuncture for depression are required in the future.

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