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Acupuncture: A Potential Therapy for Neurological and Psychiatric Disorders

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ABSTRACT

Background: Acupuncture, a practice rooted in traditional Chinese medicine for thousands of years, is increasingly recognized as a complementary therapy for neurological and psychiatric disorders.

Purpose: This review aims to explore recent advancements in acupuncture's application for treating specific neurological and psychiatric conditions and to highlight its therapeutic potential and underlying mechanisms.

Methods: The review synthesizes findings from extensive research and scientific studies, incorporating insights from modern neuroimaging techniques like functional magnetic resonance imaging (fMRI) and positron emission tomography (PET). It also examines the efficacy of combined modalities, such as laser and electroacupuncture.

Results: Acupuncture has demonstrated efficacy in managing neurological conditions such as stroke, neuropathic pain, and neurodegenerative diseases by enhancing cerebral blood flow, promoting neuroplasticity, and providing neuroprotection. Its application in psychiatric disorders, including anxiety, depression, and post-traumatic stress disorder (PTSD), has shown promising outcomes. These therapeutic effects are mediated through mechanisms involving the autonomic nervous system, decreased inflammation, and neurotransmitter regulation. Combining acupuncture with modalities like laser and electroacupuncture has expanded treatment options and enhanced efficacy.

Conclusion: Recent advancements underscore acupuncture's promise as an effective adjuvant therapy for neurological and psychiatric conditions. However, challenges remain in standardizing procedures and refining study designs to better define specific mechanisms and optimize therapeutic parameters. Continued research is essential to establish acupuncture as a reliable treatment option for improving patient outcomes.

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1. Introduction

Acupuncture is a non-pharmacological therapeutic modality with demonstrated efficacy in managing a variety of conditions, including pain, nausea, allergies, hot flashes, dyspepsia, respiratory disorders, mental health issues like anxiety and depression, and tobacco dependence. Its mechanisms, still under investigation, suggest it modulates pain perception, enhances circulation, promotes neuroplasticity, and influences neuroendocrine and immune systems. Generally considered safe when performed by trained professionals, its side effects, such as mild bruising or soreness, are rare and transient. Acupuncture is particularly effective for chronic, non-malignant conditions like musculoskeletal pain and tension-related disorders, with improvements often observed after multiple treatments. While the number of high-quality randomized controlled trials remains limited, ongoing research continues to validate its clinical benefits and refine its applications (Kawakita & Okada, 2014).

Despite its historical association with Oriental medicine, acupuncture therapy has recently gained recognition in complementary and alternative medicine as a potentially helpful approach with solid scientific support. A distinguishing feature of eastern medicine is its distinctive pathophysiological theory of illness, which highlights the circulation of qi, or energy. A core principle of Oriental medicine is the lack of a distinct separation between the body and the soul, referred to as "mind-soul unity" in

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Kampo medicine. Psychogenic diseases are conceptualized as disorders resulting from an inadequate flow of chi; this interpretation remains valid even when Western medicine fails to identify the exact etiology of the illness through advanced diagnostic techniques of the body or brain. The attributes of qi and the systems that regulate it still need to be clarified. Nevertheless, comprehending the concept of qi is crucial for understanding humans as self-regulating entities (Wolf, 1964).

Acupuncture is based on stimulating particular body points using fine needles or pressure. This therapeutic method originates from traditional Chinese medicine (TCM), which is fundamentally based on the philosophies of Taoism and Confucianism. This idea posits that qi, meaning "vital energy," encompasses the yin/yang dualism that pervades all physical reality and is harmonised when in optimal condition (Huang *et al.*, 2018). The concept of qi is founded on five elements: metal, wood, water, fire, and earth. An excess or barrier of any kind obstructs this vital force. The objective of acupuncture is to alleviate blockages or reduce excess qi circulating through specific meridians in the body. This perspective characterizes health as the integrated operation of well-being rather than only the lack of illness (Anderson *et al.*, 2019). Symptoms are not isolated; each symptom manifests in connection to a specific excess or obstruction. Restoration of connection and overall well-being is accomplished through qi balancing (Song *et al.*, 2018). Although originating in Traditional Chinese Medicine, it was introduced to the West through other Asian countries, especially Korea and Japan. Despite Osler's references to acupuncture in his medical texts from the 1700s, many perceive it as a relatively novel concept. It has historically been viewed as an alternative therapy rather than an integral part of established medical practice (Scharf *et al.*, 2006). It has been utilised by approximately 1.5% of Americans at some point, and it is available at numerous esteemed academic medical institutions nationwide (Manheimer *et al.*, 2005). Acupuncture is rarely employed as a substitute for traditional medical treatment; rather, it is utilised in conjunction with or as an adjunct to such therapies (Linde *et al.*, 2005). A multitude of research has demonstrated its effectiveness in alleviating headaches, myofascial pain, osteoarthritis-associated knee pain, and both acute and chronic back pain (Mayhew & Ernst, 2007). It is essential to recognise the significant placebo effect. Conviction possesses potency. Multiple studies indicate that sham acupuncture can be significantly beneficial in alleviating pain across various diseases. It is an essential alternative treatment approach due to its generally positive patient outcomes, minimal side effects, and negligible financial burden on the healthcare system (Lao *et al.*, 2003).

Clinical research is increasingly focusing on the attributes of Japanese acupuncture techniques, such as superficial needling without de-qi sensation, in light of the sham treatments utilised. This article provides an overview of contemporary studies about acupuncture points, the mechanisms underlying acupuncture's benefits, and the evidence supporting its safety and efficacy in managing chronic pain, specifically focusing on lower back pain. Recent applications are examined, with new research on the effects of acupuncture therapy on several psychogenic disorders, including PTSD, anxiety, and depression (Ernst & White, 2001).

2. Unveiling the Mechanisms: How Acupuncture Therapy Works

The inaugural scientific inquiry into the mechanism of acupuncture commenced about 1950 when a team from Peking University released a significant pharmacological study. They established that acupuncture necessitates a 15–20 minute induction period to elicit an analgesic effect and proposed that chemicals may contribute to these effects (Kawakita *et al.*, 2006).

Endogenous opioid peptides (EOPs), such as enkephalins and beta-endorphins, and diffuse noxious inhibitory controls (DNIC) play critical roles in pain modulation and broader physiological processes. EOPs bind to opioid receptors to reduce pain transmission in the ascending pain pathway, producing analgesic effects, while DNIC inhibits pain through spatial summation, a process mediated by EOPs. These systems are not only integral to pain relief but also contribute to stress resilience, emotional regulation, and cardiovascular protection, showcasing their importance in maintaining homeostasis. The relationship between DNIC and cardiovascular activity, where greater cardiovascular responses to noxious stimuli correlate with enhanced DNIC, highlights the integrated nature of these systems. Together, EOPs and DNIC underscore a sophisticated mechanism for pain modulation and adaptive physiological responses, offering insights into potential therapeutic applications for pain management and stress-related conditions. Endogenous opioid peptides (EOPs) are seen as strong candidates for involvement in the mechanism of acupuncture, as naloxone, an opioid receptor antagonist, mitigates electro-acupuncture analgesia (EAA) (Taguchi, 2008). Moreover, EOPs have been observed to elevate in cerebrospinal fluid (CSF) or human plasma after EAA. To illustrate the frequency-dependent participation of distinct endogenous opioid peptides (EOPs) in electro-acupuncture (EA)-induced analgesia, Han's team at Peking University utilised multiple methodologies to pinpoint the specific opioid receptors and their endogenous agonists (Pomeranz

& Chiu, 1976). Han established that mu- and delta-opioid receptors are stimulated by the release of enkephalin, beta-endorphin, and endomorphin in supraspinal central nervous system regions. Still, dynorphin interacts with kappa opioid receptors in the spinal cord to induce high-frequency (100 Hz) excitatory amino acid activity (Sjölund *et al*., 1977).

Patients attending acupuncture clinics often report instant pain relief, perhaps attributable to the gentle manipulation of the fine needles. Consequently, alternative pathways must be evaluated to elucidate the immediate advantages of acupuncture. A plausible explanation for the immediate analgesic effect of conditioned stimuli is diffuse noxious inhibitory controls (DNIC) (Han, 2003). Initially, this was reported based on tests conducted on anaesthetised rats. DNIC indicates that trigeminal caudalis and spinal dorsal horn neurons can immediately inhibit pain transmission in response to any noxious stimuli presented to any body region. As Bing *et al*. (1991) successfully demonstrated that manual acupuncture to the Zusanli (ST36) may elicit DNIC-like suppression, which naloxone can partially prevent. The DNIC mechanism requires thin afferent fibers, namely A-delta and C fibers, activated by painful pinches, immersion in hot water, or injections of analgesic medicines into muscle. The afferent DNIC input is thus supplied by nociceptors that react to mechanical, thermal, and chemical stimuli. These receptors are located in the entire body's muscles, viscera, and skin. The characteristics of polymodal receptors (PMR) are closely correlated with these afferent inputs (Bouhassira *et al*., 1987).

3. Comprehending "Acupuncture Points"

Acupuncture points are considered to be the most crucial components of therapy for the purpose of diagnosis and treatment. Unfortunately, no concrete evidence has been found to support the presence of its sites, despite several studies being carried out to assess their significance from an anatomical or histological perspective. Soreness and palpable hardenings, among other physiological characteristics of sites, are believed to be caused, at least in part, by nociceptors' sensitization to their effector functions. The use of acupuncture induces in the patient a distinct sensation called de-qi. Although the de-qi feeling is believed to be essential to acupuncture's efficacy, it is uncertain which afferent fibers and receptors generate this sensation. Injecting local anesthetics into a muscle nerve bundle innervating the Ho-ku (LI4) acupuncture sites completely abolished the de-qi caused by its manipulation (Kawakita *et al*., 2002).

Traditional Chinese textbooks refer to the location on the body called the ah-shi point—the site where a needle is inserted to elicit a vocal response in reaction to pain—as an acupuncture point. Put another way, discomfort is a physiological feature of acupuncture sites. As our previous study clearly demonstrated, Japanese acupuncturists often employ tender points and acupuncture sites in clinical settings (Chiang, 1973). Myofascia1 pain syndrome (MPS) patients have tenderness at the circumscribed region on the palpable band, which is a feature of trigger points. When these trigger points are activated, they might mimic some referred pain patterns and phenomena that the patient may feel (Kawakita *et al*., 2005). Shah *et al*. (2015) reported that the trigger points and acupuncture sites were positioned in agreement. On the other hand, it has been demonstrated that the location of painful points and acupuncture sites in fibromyalgia patients is rather similar (Melzack *et al*., 1977). The concept of trigger points was established through modern Western medicine's approach to treating pain, without reference to traditional Chinese medicine. Uncertain pathophysiological mechanisms underlie the emergence of tender loci. One possibility is the presence of nociceptors that have been sensitive at specific locations. Yunus *et al*. (1981) modeled myofascial trigger points experimentally by repeatedly tightening the forearm muscle eccentrically, resulting in delayed-onset muscular discomfort. A sensitive localized locus established on the perceptible band. A specific referred pain pattern like that of MPS patients was elicited by applying pressure to the locus. The pathophysiology of myofascial trigger points was shown to be significantly revealed by using microdialysis on human volunteers**.** The regions underneath the active trigger sites were shown to be high in substance P and calcitonin gene-related peptide (CGRP), two peptidergic neurotransmitters, bradykinin, inflammatory cytokines (IL-6, TNF-alpha), and protons (Itoh *et al*., 2004). Undoubtedly, these results demonstrate the existence of localized inflammation underneath the trigger points.

Neurogenic inflammation can occur when the PMR is activated as substance P and CGRP, two neurotransmitters, may be produced from nerve terminals. Strong evidence suggests that the PMR is involved in acupuncture's peripheral mode of action, as demonstrated by the generation of wheal and flare responses by both moxibustion and acupuncture (Shah *et al*., 2005).

3.1. Acupuncture Therapy's Effectiveness: Data from Recent Clinical Trials

Acupuncture has been the focus of several clinical investigations; as these trials' quality has grown, so too has the quality of the data supporting evidence-based acupuncture therapy. The history of acupuncture research underwent a significant change with the advent of the German mega trials and other acupuncture studies (Kawakita & Gotoh,

1996). Cumming gave a thorough explanation of ART, ARC, COMP, GERAC, and the German Acupuncture Trials (Cummings, 2009). Furthermore, several systematic reviews and meta-analyses that have been published about the utility of therapy to treat persistent musculoskeletal pain have been updated and modified (Lee *et al*., 2013). Herein, the results of two outstanding clinical studies pertaining to low back pain—the GERAC and ART projects—were selected for presentation (Hopper *et al*., 2013; Manheimer *et al*., 2010). The three parallel arms of the GERAC investigations were sham acupuncture, real acupuncture, and conventional treatment (therapy using recommendations). The RCTs were designed to be randomized controlled trials (RCTs) (Haake *et al*., 2007). Furthermore, the RCTs for the ART project contained three parallel arms: real acupuncture, sham acupuncture, and a waiting period. To generate the de-qi sensation, authentic acupuncture combined needle manipulation with deep needling at conventional acupuncture locations. Ten treatments were carried out in a span of six weeks. Fake acupuncture involves superficial needle sticking in common non-acupuncture areas (not including established acupuncture points). In standard care, multimodal treatment regimens, including NSAID therapy, exercise, and physiotherapy, were employed to deliver optimal conventional care in accordance with guidelines. The primary end measure at six months was response rate. The criteria for this were either an improvement of 12% or more on the back-specific Hanover Functional Ability Questionnaire (HFAQ) or 33% or more on three items linked to pain on the Von Korff Chronic Pain Grade Scale (CPGS) questionnaire. The six-month response rates were 47.6% for real acupuncture, 44.2% for sham acupuncture, and 27.4% for conventional treatment. There were two significant differences between the groups: 16.8% ($P < 0.001$) for minimal acupuncture against standard therapy, and 20.2% ($P < 0.001$) for acupuncture over standard care. Acupuncture, real or false, relieves pain more effectively than conventional medicine. There were more differences seen between the groups who received real and sham acupuncture and the waiting group.

Chronic low back pain is frequently associated with musculoskeletal diseases, but the underlying reason for this pain is more complex than simply lower back tissue injury. It is a more involved process, including brain plasticity, changes in the pain-transmission system, and psychogenic problems. According to the unexpectedly low association ($r = 0.27$) between the physical condition and the clinical manifestation of low back pain, psychogenic variables are crucial components of persistent low back pain (Toyama & Nishizawa, 1972). Furthermore, the majority of the 200 patients in rehabilitation programs who had persistent low back pain did not fit the diagnostic criteria for at least some of the DSM-III-R Axis I illnesses (Waddell, 1987). The phrase "psychogenic low back pain" was created to highlight the importance of psychogenic components in these people (Polatin *et al*., 1993). Based on recommendations, the low back pain results of the GERAC experiment indisputably demonstrate that acupuncture—real or fake—offered superior therapeutic advantages over conventional treatment. NSAIDs and physical therapy were the primary types of intervention for patients in the standard-care group of the GERAC trial; no preparation for pharmaceuticals for psychological issues was part of the protocol. As a result, some of the acupuncture therapies' superior success may be attributed to their therapeutic effects on the psychogenetic elements of lower back pain. The GERAC and ART studies showed no discernible statistical difference between the real and phony groups. The non-acupuncture areas in the GERAC and ART studies received little acupuncture, which did not produce a de-qi sensation. Based on the criteria, minimum acupuncture was more successful than conventional therapy, suggesting that it is not physiologically inactive and cannot be considered a placebo intervention. To confirm the specific benefits of acupuncture, a well-designed four-arm randomized controlled study (RCT) was conducted in the USA (Yoshida & Kato, 2011). Instead of restricted acupuncture using needle insertion, a wooden toothpick punctured into the skin was utilized to replicate acupuncture as a sham intervention. A single arm was subjected to tailored diagnostic and prescription acupuncture points to investigate the significance of TCM acupuncture procedures (Chen *et al*., 2022). One arm received standard TCM acupuncture manipulation, whereas the other four arms received conventional therapy. Standardized, simulated, and tailored acupuncture proved to be more successful and long-lasting than traditional treatment for persistent low back pain. Significant improvements in clinical results resulted from these treatments, which also repeatedly shown that, when it comes to treating persistent back pain, various forms of sham acupuncture are no more successful than real acupuncture needling based on the Chinese meridian system. Both phony and real acupuncture worked better than conventional medical treatment (Cherkin *et al*., 2009). It is noteworthy to emphasize that the majority of acupuncture research have demonstrated that, while there have been no appreciable distinctions between the two, both real and fake acupuncture provide better outcomes than standard therapy. As used in the German mega trials, minimum acupuncture was considered insufficient as an acupuncture stimulation method since it does not involve the utilization of acupuncture sites and does not produce a de-qi sensation. This form of mimicked acupuncture is useless as a toothpick does not pierce the skin. However, from the perspective of Japanese-style acupuncture, it is

evident that both the minimal and the simulated sham treatments involve active stimulation (MacPherson *et al.*, 2001). The shallow insertion of the small needle sets Japanese acupuncture treatments apart. Needles used in therapy settings include press-tack and intradermal needles. In addition, no-insertion needles, or needles used to puncture the skin, are employed. Generally speaking, one does not require the de-qi sensation required for TCM (Huang *et al.*, 2022). Japanese acupuncture procedures appear similar to the minimal techniques employed in the German investigations. Proficiency in Japanese acupuncture may extend beyond selecting acupuncture points based only on anatomical specifications. Usually, limited regions are identified by various characteristics of the skin and/or subcutaneous tissues, discomfort, and localized stiffness. Several randomized controlled trials (RCTs), systematic reviews, and meta-analyses have not revealed any appreciable distinctions between real and simulated treatments in patients with chronic pain. Overall, these results have supported the theory that acupuncture has no true therapeutic value and is only a potent placebo effect. The conclusion that some types of acupuncture are nonetheless more successful than standard therapy based on recommendations, even when there are no statistically significant differences, may provide a valid foundation for this result (White *et al.*, 2001).

4. Safety and Efficacy in Acupuncture Therapy

The insertion damages tissue, improper acupuncture needle insertion can have serious adverse effects. The 1980s also saw the discovery of a serious risk: using unsterilized acupuncture needles might result in cross-infection with the hepatitis B virus. Due to a growing awareness of the need of preventing these infections by the use of single-use disposable needles, professional healthcare workers have largely eliminated these infections in acupuncture treatments.

Prospective safety evaluations of acupuncture conducted in the UK, Germany (White *et al.*, 2001), and Japan (Melchart *et al.*, 2004) have already made a wealth of reliable information about the adverse effects of acupuncture treatments available. Adverse events like pneumothorax, depression exacerbation, acute hypertensive crisis, vasovagal reaction, and asthma attack with hypertension and angina were only reported six times in a more extensive German study involving over 9000 German doctors administering 760 000 acupuncture treatments (Witt *et al.*, 2009). Another large investigation of 2.2 million continuous acupuncture sessions revealed that the two side effects in two individuals were pneumothorax and lower limb nerve injury (Yamashita & Tsukayama, 2008). Nonetheless, a comprehensive evaluation showed that, on average, one in 1200 individuals who have used NSAIDs for at least two months may pass away from stomach-duodenal issues. Use of NSAIDs has also been linked to perforated gastroduodenal ulcers and internal hemorrhage (Tramèr *et al.*, 2000; Zhang *et al.*, 2010). Numerous prospective large-scale assessments have shown that acupuncture is safe and seldom results in deaths or other negative side effects.

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6. Unlocking the Potential of Acupuncture in Treating Psychogenic Disorders

Before acupuncture therapy is approved as a treatment for psychogenic diseases, sufficient evidence must be gathered. Systematic reviews of well-conducted RCTs and meta-analyses have long been recognized to provide the most substantial evidence for evidence-based medicine. We provide brief reviews of the body of research on the relationship between acupuncture therapy for psychogenic disorders and the outcomes of systematic assessments of depression, anxiety, and post-traumatic stress disorder

(PTSD). The theoretical frameworks used in the research to carry out meta-analyses and systematic reviews were similar. A comprehensive search for references relevant to the study subjects was conducted using a range of databases, and a sufficient number of publications meeting the inclusion requirements were discovered. The details found in the selected sources were examined in further detail. When possible, the patient data were aggregated for meta-analysis.

Figure 1 provides a brief summary of the findings from systematic reviews and meta-analyses of acupuncture clinical trials for the treatment of depression, anxiety, and PTSD.

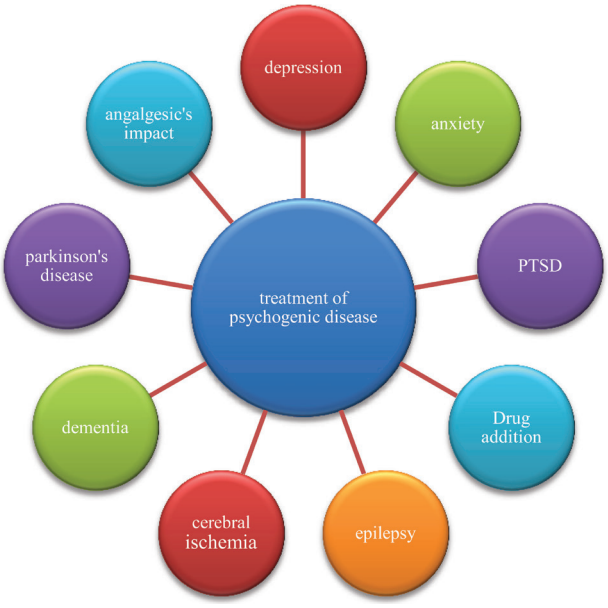

Figure 1: Treatment of Psychogenic Disease Condition by Acupuncture.

6.1. Unlocking the Potential of Acupuncture in Managing Depression: A Path to Mental Wellness

A thorough assessment and meta-analysis of 207 clinical studies, including the use of acupuncture for the treatment of depression, was completed in (Ernst *et al.*, 2011). Thirteen RCTs of post-stroke depression (PSD, n = 1680) and twenty RCTs of major depressive disorder (MDD, n = 1998) were included in the meta-analysis as well. When combined with antidepressants, acupuncture was just as effective as medication alone in improving clinical response and lowering the severity of symptoms related to major depressive disorder (MDD). On the other hand, it performed no better than fake acupuncture in terms of efficacy. The idea that antidepressants and therapy might treat MDD better than just antidepressants on their own was not sufficiently established. Acupuncture fared better than waiting controls and antidepressants in terms of improving PSD symptoms and reactivity. The researchers concluded that this therapy is a safe and efficient alternative for treating both MDD and PSD. Its efficacy in treating various forms of depression is uncertain. A systematic review of systematic reviews produced a critical evaluation intended to bolster clinical judgments. Eight systematic reviews turned up 71 primary studies. Five assessments had a positive result, while three produced a negative one. The positive reviews and most of the encouraging original research came from China (Pilkington *et al.*, 2007). The authors concluded that there is still disagreement on the effectiveness of this therapy as a depression treatment.

6.1.1. Disorders Related to Anxiety and Worry

Ten RCTs for a systematic review (Kim *et al.*, 2013). Four RCTs looked at the effectiveness of therapy in treating anxiety neurosis or generalized anxiety disorder, while six RCTs looked at anxiety during the perioperative phase. Every study on anxiety neurosis or generalized anxiety disorder showed promising outcomes; however, the articles lacked detailed methodological details. Studies have generally shown an improvement in the reporting of perioperative anxiety. In particular, auricular acupuncture has been demonstrated to be more useful than acupuncture at sham locations and may initially be just as successful as drug therapy. The trial findings did not support a firm conclusion, even if acupuncture showed promise in treating anxiety neurosis or generalized anxiety disorder. There isn't much evidence to support the use of ear acupuncture for managing perioperative pain.

6.2. Unraveling the Therapeutic Potential of Acupuncture in Managing PTSD

A study provided the first thorough assessment and meta-analysis of acupuncture as a PTSD treatment. Out of the 136 potentially relevant references that were discovered throughout their systematic review, 16 studies were evaluated. In the end, it was found that four RCTs met the criteria for inclusion. All four research studies employed a parallel-group design, and two of them were based on calculations of sample sizes. Throughout the four RCTs, a total of 543 PTSD patients got treatment for one to twelve weeks (Tan *et al.*, 2019). In a high-quality RCT, the efficacy of acupuncture was evaluated in relation to waitlist control and cognitive-behavioral therapy (CBT). Acupuncture therapy surpassed CBT in terms of statistical significance, but there were no differences between the two treatments. The therapeutic advantages of cognitive behavioral therapy and acupuncture are similar in terms of effect sizes. There were no statistically significant

differences between the groups in an RCT comparing the efficacy of oral SSRI treatment with electroacupuncture. This study's main finding—which was backed up by a meta-analysis and one outstanding RCT—was that this therapy is effective in treating post-traumatic stress disorder (PTSD). It is shown that, despite the lack of a statistically significant difference in the effectiveness of acupuncture and CBT, the latter was statistically superior to the waitlist control. The meta-analysis showed that acupuncture plus moxibustion was a more effective treatment for PTSD than oral SSRIs. But the results should be viewed with caution as the meta-analysis was based on one RCT that was of medium quality and one that was of low quality. Since there were only two RCTs in the meta-analysis, there was insufficient data to draw a firm judgment on the efficacy of acupuncture for PTSD, despite the therapy appearing to be promising.

6.3. Harnessing Acupuncture: A Natural Approach to Combating Drug Addiction

In addition to its detrimental emotional impacts, withdrawal produces undesirable psychological side effects, including anxiety and hopelessness. Numerous studies have demonstrated that stopping medicine produces behavioral changes in animals as well as anxiety and depressed symptoms in humans. Acupuncture at HT7 may reduce anxiety-like behavior that follows nicotine withdrawal by modulating corticotrophin-releasing factor in the amygdala, as shown by Alaee *et al*. (2023). Elevations in this component may also contribute to the depressed symptoms associated with quitting smoking. Even after abstaining for a while, readministration of several psychoactive substances, including cocaine and morphine, may have a stronger impact than the original dosage alone (Mohammadzadeh *et al*., 2017). An enhanced locomotor response to a second drug injection (Wei & Hsieh, 2020) suggests that this process, known as behavioral sensitization, may have an impact on the development of drug addiction and drug-induced psychosis. DA neurotransmission has been linked in several studies to the development and manifestation of behavioral sensitization brought on by repeated exposure to cocaine or morphine. The research's authors unquestionably demonstrated that acupuncture at the HT7 point significantly reduced the behavioral sensitization brought on by recurrent cocaine use and that tyrosine hydroxylase expression was elevated in the ventral tegmental region of the central dopaminergic pathways. The central DA pathway's nucleus accumbens postsynaptic neurons' increase of dopamine (DA) synthesis and activity is closely linked to repeated morphine-induced behavioral sensitization.

6.4. Unlocking Acupuncture's Potential: Managing Persistent and Uncontrollable Epilepsy

Epilepsy is a frequently occurring neurological ailment marked by seizures and a significant signal of a major brain disease. Things do not look good. As kainic acid (KA) injections intracerebrally into the rat hippocampus or amygdala matched the characteristic histological abnormalities found in epileptic patients, the AMSRC researchers hypothesized that this may be a model of temporal lobe epilepsy.

Furthermore, a study has shown that acupuncture lowers glutamate decarboxylase-67 expression and KA-induced hippocampal cell death as well as epileptic convulsions. Immunohistochemistry and Western blotting revealed that acupuncture at HT8 decreased the expression of c-Fos and c-Jun produced by KA in the hippocampal regions, as well as the rate of neural cell death and the severity of KA-induced epileptic convulsions (Barreto *et al*., 2011). Electroacupuncture and auricular acupuncture demonstrate promising therapeutic potential in epilepsy management through various mechanisms. Electroacupuncture at the Zusanli point (ST36) has been shown to reduce seizure frequency and severity while improving hippocampal neuron survival and reducing neuronal damage in epileptic rats (Xue *et al*., 2023). Similarly, auricular acupuncture was found to decrease brain levels of somatostatin and amino acid neurotransmitters, suggesting its role in modulating neurotransmitter balance to suppress seizures (Liao *et al*., 2017). Moreover, electroacupuncture at ST36-ST37 points increased GAD67 mRNA expression in the dentate gyrus, indicative of enhanced γ-aminobutyric acid (GABA) neuron activity (Zhang *et al*., 2021). Long-term stimulation at ear points and ST36-ST37 also attenuated COX-2 expression in the hippocampus, addressing inflammation and oxidative stress linked to seizure activity (He *et al*., 2012). Additionally, auricular acupuncture may activate the parasympathetic nervous system, which plays a key role in autonomic balance and seizure suppression (Xue *et al*., 2023). Together, these findings underscore the multifaceted mechanisms by which acupuncture may mitigate epilepsy symptoms and pathology.

6.5. Unveiling Acupuncture's Role in Cerebral Ischemia: Pathways to Neuroprotection and Recovery

For ischemia-induced hippocampus cell proliferation and death, acupuncture is a helpful therapy. Following ischemic damage, acupuncture at the Ho-Ku (LI4) and Zusanil (ST36) acupoints may be crucial in controlling

cell proliferation and apoptosis. 5-bromo-2-deoxyuridine immunohistochemistry (Lee *et al.*, 2014) indicates that enhanced cell proliferation in the dentate gyrus of the hippocampus after cerebral ischemia is a compensatory response to ischemia-induced increased apoptosis in gerbils. Studies have also examined the impact of ST36 acupoint acupuncture therapy on intracerebral hemorrhage-induced Fos expression and rat dentate gyrus cell proliferation. Consequently, acupuncture therapy decreases ischemia-induced apoptosis and cell proliferation, suggesting that it might be a beneficial intervention for stroke recuperation (Bussell, 2013). Acupuncture has demonstrated significant therapeutic effects in preclinical models of cerebral ischemia-reperfusion (I/R) injury. Studies report that it reduces infarct volume, ameliorates neurological deficits, and lowers mortality rates in rat models (Chavez *et al.*, 2017). Mechanistically, acupuncture suppresses endoplasmic reticulum (ER) stress-mediated autophagy and apoptosis by inactivating key pathways such as ATF-6, PERK, and IRE1 (Sun *et al.*, 2020). Furthermore, it enhances cerebral blood flow, strengthens blood-brain barrier integrity, and promotes neurogenesis and angiogenesis (Peplow & Martinez, 2016). These effects are accompanied by an upregulation of neurotrophic factor expression, highlighting acupuncture's multifaceted neuroprotective potential.

6.6. Exploring the Therapeutic Potential of Acupuncture in Dementia Treatment

Moderate chronic stress-related behavioral impairments, such as decreased learning and memory in the Morris water maze test and increased acetylcholinesterase reactivity in the hippocampus, may be efficiently corrected by its stimulation at the PC6 point (Lee *et al.*, 2014). After repetition of exogenous CORT in the Morris water maze test, acupuncture significantly reduced memory-associated decreases in BDNF, cyclic adenosine monophosphate-responsive element-binding protein (CREB) mRNA expression, and cholinergic immunoreactivity in the rats' hippocampal regions (Kim *et al.*, 2011). The potential for acupuncture stimulation to mitigate memory and cognitive deficits stems from the repair of cholinergic neurochemical imbalances and the control of CREB and BDNF production. Acupuncture has the potential to treat chronic stress-related memory deficits by regulating the HPA axis and slowing down their progression.

6.7. Exploring Acupuncture's Therapeutic Potential in Parkinson's Disease Management

The research team led by Park asserts that acupuncture helps people with Parkinson's disease by boosting the production of a protein that coats the skull. This was reported in a worldwide article on Oriental medicine that was published in the protein research journal Proteomics in November 2008. The findings of this study showed that electroacupuncture (EA) at acupoint Yanglingquan (GB34) protected against DA neuronal damage in the mouse PD model induced by 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) and changed the expression of proteins in the substantia nigra that are linked to cell death mechanisms after MPTP treatment (Chen *et al.*, 2023). Subsequent research revealed that 100-Hz EA at GB34 and GB39 points in the substantia nigra of the MPTP-induced Parkinson disease (PD) mouse model strongly preserved DA neuronal fiber and corrected the COX5b decrease and restored the increases in cytosolic malate dehydrogenase (cMDH), Munc18-1, and hydroxyacylglutathione hydrolase (Ho *et al.*, 2019).

The effectiveness of acupuncture in reducing neuropsychiatric symptoms (NPSs) linked to Parkinson's disease (PD) was thoroughly assessed in this extensive meta-analysis. Analysis of 13 randomized controlled studies with 719 PD patients provided insight into the possible advantages of this therapy as a therapeutic approach. According to the Parkinson's Disease Sleep Scale (PDSS), the outcomes showed that this therapy significantly improved sleep quality compared to medicine alone or sham acupuncture. Furthermore, the results of the Unified Parkinson's Disease Rating Scale (UPDRS) indicated that this therapy was beneficial in treating the behavioral and psychological changes linked to Parkinson's disease (PD), especially in the areas of motor and total scores. Notably, the Epworth Sleepiness Scale (ESS) and Parkinson's Disease Questionnaire-39 (PDQ-39) did not show any statistically significant changes in the research. The results for anxiety and depression did not differ much, but the authors stress the need for more study to fully understand these domains' intricacies and create focused treatment plans. Overall, this meta-analysis highlights how acupuncture may improve the quality of sleep and improve different aspects of the overall state of patients with Parkinson's disease (PD), highlighting the need for more research and development of its therapeutic uses in the area of neuropsychiatric symptoms in Parkinson's disease (Chang *et al.*, 2014).

6.8. Exploring the Analgesic Effects of Acupuncture: Mechanisms and Impact on Pain Relief

In the mouse formalin test and the rat chronic constriction injury neuropathic pain paradigm, diluted bee venom acupuncture greatly increased clonidine-induced analgesia indicating that acupuncture therapy combined with low-dose clonidine reduces the side effects of clonidine. It also

implies that a new approach to pain management could be feasible. These results suggest that, in order to improve analgesia and minimize adverse effects, acupuncture stimulation in conjunction with a reduced dosage of a 2-adrenoceptor agonist, such as clonidine, may be a more effective way to manage pain. In the later phases of the formalin test, a synergistic suppression of pain responses was revealed by a low-dose intrathecal injection of fluor citrate plus a low-dose injection of diluted bee venom at ST36. Additionally, formalin-induced elevation of glial fibrillary acidic protein, an astrocytic marker, in the spinal cord. The benefits of moxibustion heat combined with this therapy are what make warm-needle acupuncture (WNA) treatment advantageous. Pungsi (GB31) acupuncture effectively alleviated formalin-induced pain behavior when WNA was given beforehand (Mudimela *et al.*, 2022). The WNA procedure raised c-Fos levels, but WNA stimulation and pretreatment without needle insertion prevented c-Fos from being expressed in the spinal cord's superficial dorsal horn. A numbing impact on the withdrawal reflex following nerve damage was seen when EA at ST36 and SP9 reduced neuronal nitric oxide synthase immunoreactivity in the superficial layer of the spinal cord. Rats' c-Fos expression and flinching responses were reduced by low-frequency (1 Hz, 3 mA) EA stimulation at BL60 during the late phase following formalin administration. These studies demonstrate a fast rise in cytokine production in the dorsal root ganglia and injured peripheral nerves of neuropathic rats following exposure to extracellular arachidonic acid (EA). Moreover, they suggest that chronic pain, which reacts to acupuncture stimulation, namely epidermal growth factor (EGF), may be associated with elevated levels of cytokines such as IL-1, IL-6, and tumor necrosis factor.

7. Conclusion

In summary, the analysis of this examination's study indicates a noteworthy advancement in the use of acupuncture to treat neurological and psychiatric disorders. The meta-analysis clarified acupuncture's notable effectiveness in improving a range of patient well-being factors, with a special emphasis on Parkinson's illness. The documented improvement in psychological moods highlights acupuncture's therapeutic promise in addressing complex neuropsychiatric symptoms, overall Parkinson's symptoms, and sleep quality as shown by PDSS and UPDRS scores.

Although the results show promise, the study also identified areas that require more research. Notably, the absence of statistically significant improvements in outcomes related to quality of life, anxiety, and depression highlights how complex these factors are when combined with acupuncture treatment. This emphasizes the necessity of further study to sort through the intricacies surrounding psychological well-being and improve and customize acupuncture treatments to more successfully target particular areas.

This therapy is a viable treatment option for neurological and psychiatric disorders since it is a comprehensive, non-invasive therapy. The field's research environment is changing, which encourages a wider knowledge of acupuncture's function in improving overall health and quality of life for people dealing with a variety of neurological and psychiatric illnesses. This gives promise for novel and successful therapies. In order to further enhance its incorporation into mainstream healthcare and give patients more efficient alternatives for treating the complexity of various illnesses, further research and validation of the treatment modality are necessary.

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Maneesh Mohan: Investigation, Writing - Review and Editing
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