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Applying the Power of the Mind in Acupuncture Treatment of Pain

Jian Kong, MD, MS, MPH, and Maya Nicole Eshel, BA

ABSTRACT

Background: Healing is a complicated process that can have several components including the self-healing properties of the body, the nonspecific effects of treatment (e.g., the power of the mind), and the specific effects of an intervention. This article first discusses the brain imaging studies on placebo acupuncture analgesia and the modulation effects of expectancy on real acupuncture in healthy subjects. Then, it introduces some attempts to translate findings from healthy subjects to patient population using power of the mind as a way to enhance acupuncture's treatment effects on chronic pain. After that, a new alternative method which merges acupuncture and imagery, while also drawing on power of the mind, is presented. Finally, the specific effects of acupuncture are discussed.
Conclusions: Elucidating the mechanism underlying power of the mind would provide new opportunities for boosting the therapeutic effect of acupuncture treatment and furthering the development of new alternative interventions.

Keywords: nonspecific effect, acupuncture, brain imaging, pain, placebo, imagined acupuncture

INTRODUCTION

Healing is the goal of medicine and it can involve three key components: (1) the self-healing properties of the body (i.e., the power of the human body); (2) the nonspecific effects of treatment (i.e., the power of the mind); and (3) the specific effect of a physical or pharmacologic intervention (i.e., the power of medicine). Since ancient times, the power of the mind in healing has been recognized by both Chinese and Western Medicine. For instance, the *Huang Di Nei Jing* (the ''bible'' of acupuncture and Chinese Medicine) suggests that clinicians should not treat patients who do not trust the treatment.[1] Hippocrates, ''the father of medicine,'' acknowledged that positive engagement with the physician is critical for positive outcomes.[2]

Experimental and clinical studies have also demonstrated the role of nonspecific effects in acupuncture treatment. For instance, a meta-analysis of acupuncture for chronic pain has confirmed this theory, suggesting that factors in addition to the specific effects of needling are important contributors to the therapeutic effects of acupuncture.[3] In an expansive study to determine if all placebo effects were equal, Kong and colleagues found that there were no significant associations among placebo pills, sham acupuncture, and cue conditioning effects.[4] This suggests that individuals might respond to unique healing rituals in different ways and that the placebo response might be a complex behavioral phenomenon with properties that comprise a state rather than a trait characteristic. At the same time, the researchers found a significant association between real and sham acupuncture treatments, suggesting that the nonspecific effects of acupuncture might contribute to the analgesic effect observed in genuine acupuncture analgesia.

This article introduces some work performed in the current authors' laboratory on the brain mechanisms of acupuncture's placebo/nocebo effect, presents translational research on attempts to boost the effect of acupuncture treatment and develop new interventions by applying the power of the mind, and offers insight on the specific effects of acupuncture. It is worth noting that the literature on these

Department of Psychiatry, Massachusetts General Hospital, Harvard Medical School, MA, USA

topics is extensive, and readers would benefit from articles by other investigators to gain a more-comprehensive picture of acupuncture, expectancy, and their interactions.

THE POWER OF NONSPECIFIC EFFECTS IN HEALTHY SUBJECTS

One example demonstrating the power of the mind is the nonspecific effect or placebo/nocebo effect. In an earlier study, Kong and colleagues tested the effects of a validated sham-acupuncture needle to investigate the brain network involved in placebo analgesia.[5] The researchers found that, after placebo acupuncture treatment of the forearm, subjective pain-rating reduction on the placebo-treated side was significantly greater than on the control side. Functional magnetic resonance imaging (fMRI) signals between pre- and post-treatment showed significant fMRI signal increases in brain areas associated with pain modulation/evaluation, such as the rostral anterior cingulate cortex, but no significant decreases in pain-sensitive areas were detected. This finding was consistent with a 2018 meta-analysis,[6] in which the researchers found that placebo treatments had very small effects (decreased fMRI signals) on the ''neurologic pain signature,'' a validated measure that tracks levels of nociceptive pain. Based on these findings, the researchers proposed that placebo treatments affected pain via brain mechanisms largely independent of bottom-up nociceptive processing and that placebo analgesia was likely to result from multiple brain pathways and mechanisms.

In another study, other researchers investigated the effect of negative expectancy and found that it can produce a pain-rating increase after placebo acupuncture (hyperalgesic nocebo effect), as well as an fMRI-signal increase in brain regions associated with anxiety about pain (such as the hippocampus) and the brain regions involved in the affective aspect of pain (such as the dorsal anterior cingulate cortex [ACC] and insula).[7] This result showed that expectancy could modulate pain processing in two directions. Positive expectancy could reduce pain experience, while negative expectancy could increase pain experience, and the two effects are associated with different brain circuits.[8]

APPLYING MIND POWER TO ENHANCE ACUPUNCTURE'S EFFECT ON CHRONIC PAIN

Building on the abovementioned research, subsequent studies indicated three findings. First, conditioning positive expectations can amplify acupuncture analgesia, as detected by both subjective pain sensory-rating changes and objective fMRI-signal changes in response to calibrated noxious stimuli.[9] Second, acupuncture analgesia and placebo analgesia show comparable magnitudes of behavioral efficacy but with different patterns of associated brain activation.[1] Finally (third), different brain networks are involved with the expectancy effects in verum acupuncture, compared to sham acupuncture, in healthy subjects.[10]

Kong and colleagues have started to apply findings from healthy subjects to acupuncture treatment for chronic pain. These researchers found that enhancing expectancy using condition-like expectancy manipulation can significantly increase the therapeutic effect of acupuncture knee-pain treatment after 4 weeks, compared to identical treatment without expectancy manipulation, which demonstrates the potential of expectancy in acupuncture practice.[9]

In other studies, researchers applied a context-manipulation model (combining verbal suggestion and specific rituals such as feeling each patient's pulse and inspecting the patient's tongue) in a cohort of patients with chronic low-back pain (cLBP) to test if enhancing the doctor–patient relationship can increase the expectancy and treatment effect of acupuncture. The researchers did not detect significant differences in clinical outcomes or expectancy scores between the high- and low-context groups.[11,12]

Taken together, these results suggest that boosting nonspecific effects (by applying the power of the mind) might shed light on enhancing treatment effects.[13] Nevertheless, enhancing expectancy and gaining patients' trust is a complicated process, and while warmth and empathy may be two of several factors that can influence patients' expectancy/belief, they do not guarantee increased expectancy/belief on their own.[11]

COMBINING IMAGERY AND ACUPUNCTURE TO RELIEVE PAIN

A nonspecific effect/placebo effect is just one example demonstrating the power of the mind. Imagery is another example. The use of imagery to treat illness is one of the oldest medical practices.[14,15] Currently, it is commonly used as a therapeutic method for addressing many disorders, such as chronic pain.[16–19] A large body of literature suggests that common brain areas are activated during direct and vicarious (observational) experiences.[20] For example, observing others' experience of pain can activate a network similar to the one that is activated when one experiences pain directly.[21–29] Furthermore, investigators have found that imagined painful scenarios from a first-person perspective can be more-vivid, less-difficult, and less-disembodied than scenarios imagined from a third-person perspective,[25,30] and can produce stronger fMRI signal increases at S-2 and insula.[30]

As an invasive treatment, acupuncture involves needle insertion and manipulation. Literature suggests that De Qi (sensations—such as soreness, aching, and dull pain—induced by acupuncture-needle manipulation) are crucial

for treatment effects.[31–33] To the extent that these acupuncture sensations can be elicited by watching a video of acupuncture treatment and imagining the treatment, one would expect brain-activity changes that overlap with changes produced by the real acupuncture-needle manipulation to occur. Indeed, this has been demonstrated by a previous brain-imaging study in which investigators found that visualizing images of acupuncture needle stimulation[34] produced overlapping fMRI signal changes in the brain at the anterior insula, cingulate cortex, and periaqueductal gray (PAG).

Recently, Cao and colleagues combined acupuncture and imagery to develop a new treatment method—video-guided acupuncture imagery treatment (VGAIT). During VGAIT, participants watch a video of acupuncture that has been previously administered to their bodies and imagine it being concurrently applied. VGAIT increased pain thresholds significantly in healthy subjects. The brain activity at the insula and rostral ACC—key regions in pain processing and modulation—was associated with analgesia evoked by real acupuncture and VGAIT.[35] In a recent following study, these researchers found that acupuncture decreased regional homogeneity (ReHo) and functional connectivity (FC) in sensorimotor areas, whereas VGAIT increased ReHo in basal ganglia (BG; i.e., putamen) and FC between the BG subcortical network and the default-mode network. A multimodality fusion approach with preintervention ReHo and gray-matter volume (GMV) as features showed that variability in acupuncture responses was associated with ReHo and GMV in BG, whereas VGAIT responses were associated with ReHo and GMV in the anterior insula. These results suggested that, through different pathways, both real acupuncture and VGAIT can modulate brain systems to produce analgesic effects.[36]

In a more-recent pilot study, Cao and colleagues found that 1 month of VGAIT (6 treatments) reduced the severity of cLBP significantly.[37] A comparison between this study[37] and a previous acupuncture study from the current author's laboratory using the same treatment paradigm showed that VGAIT produced similar effects to real acupuncture, and marginally greater low back-pain relief, compared to sham acupuncture.[11,12] These findings indicate a new way to apply the power of the mind in pain management. VGAIT may be a promising supplementary treatment for cLBP and other pain conditions, particularly during the COVID 19 pandemic, as VGAIT may be applied remotely.

SPECIFIC EFFECTS OF ACUPUNCTURE TREATMENT

Emphasizing the power of the mind does not mean that there is no specific effect induced by acupuncture, but rather that comparatively investigating placebo effects and acupuncture effects can enhance understanding acupuncture's effect. For instance, in a previous study of patients with knee osteoarthritis, Gollub and colleagues found regional coherence increased in the left postcentral and precentral gyrus in an area corresponding to the right hand (at LI 4) where electroacupuncture (EA) was applied in a verum-acupuncture group more than in a sham-acupuncture group. Conversely, compared with sham EA, during verum EA, the regional coherence significantly decreased in bilateral pain-related brain areas, including the dorsal ACC, secondary somatosensory cortex, and insula/operculum. More interestingly, there were no significant differences between verum and sham EA in the younger, healthy cohort in whom a similar treatment paradigm was used.[38]

A following study explored the role of doctor–patient relationships in acupuncture treatment for cLBP. The role of context in acupuncture treatment was not detected. However, it was suggested that verum acupuncture might simultaneously modulate the resting state functional connectivities (rsFC) of key regions in the descending pain-modulation (e.g., PAG) and reward systems (e.g., ventral tegmental area), compared to sham acupuncture.[12] In another analysis based on the same data set, machine-learning approaches were used to test if pretreatment rsFC could predict responses to both verum and sham acupuncture treatments in patients with cLBP. Pretreatment rsFC predicted symptom changes with up to 34% and 29% variances for real and sham treatments, respectively. Furthermore, the functional connectivity characteristics that were significantly predictive for verum and sham treatment differed, indicating that different networks might underlie real and sham acupuncture.[11]

In a recent study on patients with migraines, a neural marker was first identified with abnormal functional connectivity within the visual, default, sensorimotor, and frontal–parietal networks that differentiated patients with migraines from healthy controls. In addition, although both verum and sham acupuncture treatments reduced headache frequency significantly, with no significant differences between the two treatments, a significant correlation between the connectome-based marker change (pre–post-treatment) and corresponding changes of headache frequency in patients who received verum acupuncture existed.[39] However, this was not the case with sham acupuncture or wait-listed patients.[39]

Taken together, these results suggested that acupuncture is more than a placebo. Acupuncture can modulate sophisticated systems, including the descending pain-modulation system and reward networks,[12] as well as pain-related brain regions[10,40]/connectome-based markers.[39]

DISCUSSION

It worth noting that powerful nonspecific effects are not unique to acupuncture. Studies have suggested that expectancy can also modulate the effectiveness of pharmacologic

treatment significantly.[41] For instance, studies have shown that positive expectancy can enhance analgesic effect of remifentanil, while negative expectations of treatment can override all of this drug's analgesic effects.[42]

Meanwhile, as in other kinds of medicine, there is an urgent need for a theoretical development/breakthrough regarding acupuncture to improve its effect size. For instance, the emerging interest in stimulating peripheral activity to relieve conditions seeks to understand mechanisms that underlie electrical control of organ systems and how to stimulate the body's peripheral nerves to treat various disorders, which matches the basic concept of acupuncture well. Accumulating evidence suggests that transcutaneous auricular vagus-nerve stimulation can relieve symptoms of patients with varying disorders significantly, including epilepsy,[43,44] prediabetes,[45] depression,[46–48] and chronic tinnitus.[49] A recent animal study[50] has suggested that revealing the somatotopic organization and intensity dependency for driving distinct autonomic pathways may be used as a roadmap for optimizing stimulation parameters to improve both efficacy and safety in acupuncture as a therapeutic modality.

As another example, various researchers who share the current authors' group recently proposed a new method to develop scalp acupuncture (brain stimulation) protocols based on brain-imaging data analyses for different disorders such as dementia,[51] depression,[52] autism,[53] and mild cognitive impairment.[54] The basic concept of scalp acupuncture might at least partially match brain-stimulation therapies, such as transcranial alternating current stimulation and transcranial direct current stimulation. Finding a way to incorporate findings of biomedical science into acupuncture research and development while maintaining acupuncture as an independent practice remains a challenge.

CONCLUSIONS

The power of the mind (such as in nonspecific effects/placebo effects/imagery) could represent a key factor in achieving treatment effects in acupuncture (and other alternative medicine) practice. This highlights the interaction that occurs between the body and the mind. The brain might play a crucial role in reshaping the way bottom-up information is processed through top-down regulation, using complex brain systems. A skillful application of the power of the mind could shed light on boosting the therapeutic effect of acupuncture treatment and lead to development of new alternative interventions.

AUTHOR DISCLOSURE STATEMENT

Dr. Kong holds equity in a startup company (MNT) and has pending patents to develop new neuromodulation tools, but declares no financial conflicts of interest. No financial conflicts of interest exist for Dr. Eshel.

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Address correspondence to:
Jian Kong, MD, MS, MPH
Building 120, 2nd Avenue
Charlestown, MA, 02129
USA

E-mail: jkong2@mgh.harvard.edu