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Autonomic Activation in Insomnia: The Case for Acupuncture

Wei Huang, M.D., Ph.D.[1,2]; Nancy Kutner, Ph.D.[2]; Donald L. Bliwise, Ph.D.[3]

[1]Atlanta VA Medical Center; [2]Department of Rehabilitation Medicine Emory University School of Medicine; [3]Department of Neurology, Psychiatry/Behavioral Sciences Emory University School of Medicine

Current conceptualizations of the biological basis for insomnia typically invoke central nervous system and/or autonomic nervous system arousal. Acupuncture may represent a unique avenue of treatment for poor sleep by virtue of its direct effects on peripheral nerves and muscles, which, in turn, modulate autonomic tone and central activation. In this review, we summarize both basic and clinical research indicating that acupuncture exerts profound influences via a wide variety of potential neural and/or hormonal mechanisms that have great relevance for the modulation of sleep and wakefulness. We illustrate principles of acupuncture intervention applied to cases of otherwise intractable insomnia that document successful application of this component of Traditional Chinese Medicine to the treatment of poor sleep. Our review indicates the necessity for further research in the relationship between the effects of acupuncture on insomnia and autonomic regulation, which might guide better selective use of this treatment modality for insomnia.

Keywords: Insomnia, autonomic nervous system, acupuncture, mechanism

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Acupuncture is an important treatment modality in Traditional Chinese Medicine (TCM), which involves inserting and manipulating needles at a combination of points on the body (including trunk, limbs, ears, scalp, etc.) called acupoints to relieve symptoms, to achieve therapeutic effects, and/or to prevent the development of more severe medical conditions. It has been practiced for over 3000 years with beneficial clinical effects on many disorders. Because of dissimilar philosophical views on the human body, the languages used by energy-based TCM (holistic and metaphysical) and biophysiology-based Western Medicine (anatomic and empirical) are completely different. The ancient Chinese theories of "meridians" and "energy balancing" or "unblocking effects of acupuncture" have confused Western readers and often provide the basis for conventional Western medicine practitioners to express their doubts and disbeliefs. Thus, to explore the mechanisms of acupuncture using contemporary Western science may facilitate the bridging of Traditional Chinese and Conventional Western medical systems and the expansion of acupuncture application in various conditions, such as insomnia.

Our earlier systemic review focused on the clinical effects of acupuncture in treating insomnia was conducted including studies in both English and Chinese literature through July 2007,[1] with 93% of the 30 studies that met inclusion criteria showing positive treatment effects of acupuncture in improving various aspects of sleep. Improved subjective sleep outcomes included reduced sleep latency, increased sleep and wake ratio (sleep efficiency), enhanced sleep duration and quality, and resolution of insomnia symptoms. A few studies with objective sleep measurements using wrist actigraphy or polysomnography reported improvement in sleep onset latency in anxiety patients. Studies comparing acupuncture with medications all showed greater efficacy of acupuncture, although medication achieved benefit more rapidly and acupuncture required more treatments to surpass the effectiveness of medication. Maintenance of acupuncture treatment effects were found to be up to 3.5 years at follow-up. Some important notions related to clinical practice and research, such as acupoint selection, treatment paradigm, and treatment duration, were discussed in detail. However, the mechanisms underlying acupuncture's effects on insomnia are not fully understood. The current review examines the possibility that the autonomic nervous system may serve to mediate acupuncture's beneficial effects in treating insomnia.

INSOMNIA AND HYPERAROUSAL

Hyperarousal has been examined as a correlate of insomnia in cross-sectional studies,[2-4] with substantial evidence for associated pathophysiology involving both the central nervous system (CNS) and the autonomic nervous system (ANS). CNS arousal is supported by descriptive evidence suggesting that individuals with poor sleep are chronically more alert on tests of daytime alertness, such as the multiple sleep latency test (MSLT),[5-7] and have elevated measures of high-frequency electroencephalographic activity (beta or gamma range) during nocturnal sleep,[8-11] as well as experimental evidence indicating greater reactivity among individuals predisposed to poor sleep.[12] More recently, functional neuroimaging studies involving single photon emission computed tomography (SPECT),[13] positron emission tomography (PET),[14] or proton magnetic resonance spectroscopy (MRS)[15] have suggested that individuals with insomnia may have enhanced activation in particular brain regions as well. ANS arousal is supported by a long history of evidence of higher metabolic rates,[6] body temperatures,[16-18] electrodermal activity,[19] and heart rates[17,18] in individuals with chronically poor sleep, as well as studies demonstrating increased low-frequency power and decreased high-frequency power in heart rate intervals[20] in insomni-

acs. Elevated sympathetic tone is also implicated by raised cortisol levels and activation of the hypothalamic-pituitary-adrenal (HPA) axis in chronic insomniacs.[21] Elevations in the HPA may be mediated in part by corticotrophin-releasing hormone (CRH), and this neuropeptide may represent an important link between ANS and CNS activation in insomnia.[22] Taken together, these studies raise the intriguing possibility that interventions directly influencing peripheral hyperarousal and balancing sympathetic and parasympathetic tone may afford unique opportunities to successfully modify chronically poor sleep.

ACUPUNCTURE AND AUTONOMIC FUNCTION

Acupuncture represents a potentially unique and different avenue for insomnia intervention because of its direct effects on the autonomic nervous system. It has been shown to influence some known indicators of autonomic activities, such as blood pressure,[23-25] pupil size,[26] skin conductance,[27] thermography recorded skin temperature,[28,29] microneurography recorded muscle sympathetic nerve activities,[23,30] heart rate and/or pulse rate,[29,31] and heart rate variability.[27,32-34]

How acupuncture produces changes in autonomic activities remains uncertain. Traditional acupuncture requires elicitation of the Deqi ("Da Chee," literally translated "getting the energy") sensation, achieved by twisting and thrusting the needle after its insertion into an acupuncture point. It is experienced as local soreness and heaviness as well as radiating paresthesia, a sensation that can also be obtained in strong muscle contractions.[35-37] Because of such practice in traditional acupuncture, Andersson and Lundeberg hypothesized acupuncture in producing effects via sympathetic regulation in the same way as other forms of sensory stimulation or strong muscle contractions.[35] Their theory has been instrumental in understanding the pain relief effects of acupuncture needling, as well as exercise, massage, or transcutaneous electrical nerve stimulator (TENS) treatments.

However, besides generalized effects via sensory stimulation, acupuncture seems to also produce some specific effects on the autonomic nervous system, supported by experimental and clinical data, which go beyond Andersson and Lundeberg's theory. One demonstration is by *acupuncture points specificity* [32,36-38] that can account for different effects on the autonomic nervous system in different studies, such as facilitation of parasympathetic and suppression of sympathetic activities (PC-4 Ximen,[31] GV-14 Dazhui & PC-6 Neiguan,[33] EX-HN1 Sishencong,[39] BL-15 Xinshu[27]), significant increase of parasympathetic activity without effects on sympathetic activity (auricular Lung[32]), coactivation of both parasympathetic and sympathetic activities (LI-11 Quchi[32]), or increase of segmental sympathetic vasomotor activity with central sympathetic inhibition (LI-4 Hegu,[28] ST-36 Zusanli[23,36]). Another demonstration involves *stimulus type specificity*. When acupuncture was performed via electrical stimulation, rather than via manual manipulation, only the specific 2 Hz frequency of electrical stimulation, the frequency that most closely mimics the frequency of traditional manual acupuncture, produced sustained effects on autonomic activity.[29] These findings signify the uniqueness of acupuncture in achieving specific effects that cannot be achieved by other modalities that only produce generalized effects.

Although there is still uncertainty in the medical and research community regarding the effects of sham acupuncture, the understanding of both site and stimulation type specificity are particularly important in establishing a credible sham intervention, which is much more complicated than administration of a placebo tablet. Sham acupuncture has been conducted in research studies using various techniques that specifically are intended *not* to stimulate known acupuncture points as in traditional treatments. Some approaches have involved acupuncture needles penetrating skin at different depths than real acupuncture, some have used points at different locations away from real acupuncture points (usually within a few millimeters), and some have used telescopic needles to mimic the visual effects of real acupuncture. However, careful interpretation is warranted because sham acupuncture techniques may still produce generalized effects. For instance, in sham acupuncture design with a penetrating needle or with a telescopic needle pressing on skin, sensory pathways could still be activated, although the type and strength of the sensory signal may differ and vary by depths and/or locations. Some generalized physiological effects may be produced. Thus, technically it becomes exceptionally challenging to design a sham acupuncture (needle) procedure to be both psychologically believable and physiologically inactive. In one review, for example, sham acupuncture had an analgesic effect in 40% to 50% subjects as compared to 60% in real acupuncture.[40] With those nonspecific, but very real, effects, large sample sizes may be required to meaningfully compare real versus sham acupuncture.[40] Perhaps for these reasons, findings from studies using sham acupuncture controls have varied widely, even when studying a same-disease population. In our acupuncture and insomnia review,[1] we found only 5 studies that compared sham versus real acupressure/acupuncture treatments. Four of these studies demonstrated significantly greater improvements in the real acupuncture group relative to sham acupuncture and one failed to show significant difference between groups.

POSSIBLE MECHANISMS UNDERLYING CLINICAL EFFECTS OF ACUPUNCTURE

Acupuncture has also been shown to modulate the activities of sympathetic and parasympathetic nervous systems that are essential for cardiovascular function, as evidenced by its regulation of heart function,[41,42] blood pressure,[24,43] and heart rate.[29,31] This has led to its clinical use in the management of various cardiovascular diseases,[44-46] such as hypertension,[24,43] ischemic heart disease,[44] and cardiac arrhythmia.[47-49] In addition, both basic science and clinical studies have indicated that acupuncture regulates various neurotransmitters and hormonal factors, including endorphins, serotonin, norepinephrine, adrenocorticotrophic hormone (ACTH), cortisol, acetylcholine (Ach), melatonin, substance P, other neuropeptides, gamma-aminobutyric acid (GABA), and nitric oxide, all of which play major roles in sleep regulation, higher cortical function, the hypothalamic-pituitary-adrenal axis, and the somatovisceral reflexes.[50-66] These studies are summarized in **Table 1**.

The regulation of various other neurotransmitters and hormonal factors by acupuncture is complex and can exert opposite effects, depending on locations of acupoints and techniques used in clinical applications. For instance, ACTH can be elevated when CV-4 (Guanyuan) is stimulated with moxibustion (heating of acupoint) to improve immunity in tumor-bearing mice[67] but can be suppressed when acupuncture or electroacupuncture (electrical stimulation combined with acupuncture) is used to treat addiction in heroin addicts.[68] The use of acupuncture at PC-6 (Neiguan) has been indicated in cardiovascular regulation and postoperative nausea suppression,[69] and animal studies demonstrated that stimulation of this site may increase c-fos activation for serotonin in the raphe nuclei,[70] a region proximal to the area postrema implicated in nausea and vomiting. Somewhat different effects of acupuncture on serotonin were shown in a clinical study using Jin-3-needling therapy (needling at PC-6 along with other acupoints) for generalized anxiety disorder, where such treatments resulted in lower plasma levels of serotonin.[71] In chronic-stress induced depressive rats, electroacupuncture of GV-20 (Baihui) and SP-6 (Sanyinjiao) was observed to have up-regulation of both serotonin and acetyl cholinesterase activities in hippocampal region.[72] The disparate effects of acupuncture at different body regions with varying levels of acetylcholine in brain and cerebrospinal fluid have also be demonstrated in several additional studies.[73-75] Acupuncture or electroacupuncture was found to increase norepinephrine levels in brain regions, such as caudate nucleus and diencephalon[76-78] but to decrease norepinephrine levels in plasma,[77] again arguing for the complexity of its effects. Insofar as GABA is concerned, animal models have been demonstrated up-regulation of GABA expression after acupuncture, thus producing some neuroprotective effects in ischemic vascular events or experimentally induced seizures, as well as reducing alcohol withdrawal symptoms.[65,79,80]

The above-mentioned diverse and complex effects of acupuncture, in fact, argue for the superior application of acupuncture in treating diseases. Rather than a pharmacological agent acting with single-directional effect and often carrying adverse reactions, acupuncture modulates the nervous system to achieve desired balance. For instance, β-blockers can down-regulate sympathetic tone; however, due to their nonspecific and unbalanced effects on sympathetic activities, they can also cause side effects. Therefore, using propranolol to treat insomnia proved to be ineffective[81]; in addition, it has been shown to have numerous undesirable central nervous system side effects, including vivid dreams, nightmares and depression.[82,83] On the other hand, acupuncture has been widely used in treating various conditions with minimal side effects,[84] likely mediated by its regulation of the autonomic nervous system using bi-directional balancing mechanisms as mentioned above. The conditions that can be treated by acupuncture are as diverse as somatic pain,[85-87] headaches,[88] asthma,[89] inflammatory diseases,[44,90-92] nausea and vomiting,[93,94] gastrointestinal dysfunction,[55,95,96] substance abuse,[97-99] and anxiety.[100,101]

Despite this evidence, acupuncture is not a panacea and has been shown ineffective in treating some conditions or subtypes of treatable conditions that are not regulated via the autonomic nervous system, e.g., hypertension due to ligation of the renal artery (renin-angiotensin dependent),[102] or histamine induced asthma.[103] Because the autonomic nervous system can be more broadly considered as regulating biological equilibrium (instead of merely up-regulating or down-regulating particular organ systems), this may account for acupuncture's reported success in treating "opposite" conditions, such as hypotension[104,105] as well as hypertension,[24,43] and hyperfunction, as well as hypofunction of gastrointestinal motility.[106] Additionally, some evidence suggests that the effects of acupuncture are only observed when the normal biological equilibrium is disturbed, such as when baseline blood pressures are outside the normal range.[24,43] It cannot reverse severe pathological conditions beyond simple disturbances of biological equilibrium, e.g., severe arthrosclerotic disease, organ failure, or degenerative changes.

Table 1—The effects of acupuncture on various neurotransmitters and hormonal factors known to be involved in sleep regulation

Neuromodulator	Acupuncture Effects
Endorphins	Acupuncture enhances the production of endorphin for its various actions, mainly notable for pain relief.[85,107-111] Some studies suggest that the sleep promoting effects of electroacupuncture might be associated with stimulation of the opiodergic neurons to increase the concentrations of beta-endorphin and the involvement of the mu-opioid receptors.[112]
Serotonin	Acupuncture and electrical acupuncture have been associated with accelerating the synthesis and release of serotonin in the central nervous system.[52,53]
Norepinephrine (NE)	Increased level of NE in caudate nucleus and diencephalon with decreased level in plasma was observed with acupuncture.[76-78]
Adrenocorticotrophic hormone (ACTH)	ACTH serum levels can be modified by acupuncture in treating various conditions.[113,114]
Cortisol	Increased cortisol serum levels were observed with acupuncture in treating heroin addicts.[115]
Acetylcholine	Regulation of acetylcholine and cholinesterase by acupuncture has been shown in its treatment of pain.[73-75]
Melatonin	Melatonin levels have been observed to increase with certain acupoints stimulations,[116,117] and treated insomnia in anxiety subjects.[59]
Substance P	Acupuncture likely modulates substance P via opiate pathways, [118,119] to have anti-inflammatory effects[120] or to treat asthma.[121]
Gamma-aminobutyric acid (GABA)	Up-regulation of GABA expression was observed with acupuncture in treating ischemic vascular events[63] or alcohol withdrawal symptoms.[64] Release of GABA was observed with electroacupuncture in rats.[122]
Nitric Oxide	Stimulation of certain acupuncture points are observed to increase nitric oxide content in the brain and serum, which were associated with sleep promotion clinically.[123,124]

CASES DEMONSTRATING POTENTIAL APPLICATION OF ACUPUNCTURE IN TREATING INSOMNIA

Introduction of acupuncture into sleep medicine practice must await well-designed randomized clinical trials showing unequivocal evidence of improvement with subjective as well as objective outcome measures, with close attention paid to the control of nonspecific effects of acupuncture using careful sham design. Selection of measures that assess the mediating mechanism(s) via which acupuncture acts should be employed. Only a few such studies are available to date (see Huang et al.[1] for review), including a recent randomized, single-blinded clinical trial using electroacupuncture versus non-electrical placebo needles in treating mainly middle-aged adults with chronic moderate insomnia.[125] Issues of number of treatments, type of acupuncture, number of sessions, and patients' ages and range of comorbidities all remain to be clarified. Nonetheless, we offer in this review three clinical cases to demonstrate the effects of acupuncture in clinical practice that achieved some amelioration of otherwise intractable insomnia. The patients in these cases were treated by the first author (WH), a board-certified, American-trained physiatrist with advanced certified acupuncture training in China. The clinical improvements in sleep were demonstrated using various subjective and/or functional assessments, and in one case objective actigraphic verification. Because a case series of treated patients cannot substitute for a randomized clinical trial, a demonstration of efficiency or clarification of mechanisms must await such work. Rather, our intention here is to illustrate to readers the clinical effects observed in practice using acupuncture treatments and thus the necessity for further work to be conducted with more rigorous examination, including exploration of its possible mediating mechanism as hypothesized in our review.

Case #1

A 55-year-old Caucasian female presented with sleep difficulties 6 nights/week for a year. She used melatonin, lorazepam (2-4 mg), and/or acetaminophen pm nightly to help her sleep. She reported her sleep difficulties related mostly to stress, although sometimes to knee pain as well. Because of her work as a magazine editor, she often read and wrote in bed, had very irregular sleeping hours, and reported significant trouble falling asleep, as well as trouble staying asleep. The patient had never undergone polysomnography, and it is unclear whether she might have had obstructive sleep apnea. Past medical history was significant for ovarian cancer, status post chemotherapy 5.5 years ago, bilateral foot neuropathy as a result of chemotherapy, bilateral moderate knee osteoarthritis, hypertension, depression, and borderline diabetes. She had sulfa allergy and was taking regular medications for hypertension (ramipril and hydrochlorothiazide), depression and neuropathy (duloxetine), and hypercholesterolemia (atorvastatin). She lived with her husband and denied any use of tobacco, alcohol, or illicit drugs. Her body mass index (BMI) was 29.8.

At the time of presentation, her Pittsburgh Sleep Quality Index (PSQI) was 17, indicating very poor subjective sleep. She had 2 nights of sleep monitoring with sleep diary and wrist actigraph before the start of acupuncture. She recorded 6 h of estimated sleep for the first night and 4 h for the second night, and used 4 mg lorazepam the first night and 2 mg lorazepam the second night to assist with sleep. Wrist actigraph recorded sleep efficiency (SE) 60.5%, total sleep time (TST) 315 minutes, and wake time after sleep onset (WASO) 58.5 minutes, averaged across the 2 nights. Her depression score as evaluated by the Geriatric Depression Scale (GDS)[126] was 24, suggesting substantially depressive mood.

Acupuncture points[127] selection was based on Traditional Chinese Medicine theory for treatment of sleep disturbances with the least overlapping treatment effects for other conditions, e.g., pain. Thus, Ex-HN-3 (Yintang), Ex-HN-22 (Anmian), HT-7 (Shenmen), KI-3 (Taixi), and LR-3 (Taichong) were selected. Provider and subject interaction time was 45-60 minutes each session, including brief history and exam and acupuncture treatment. A total of 12 sessions were conducted twice a week for 4 weeks, followed by once a week for 4 weeks. Sterile, single-use disposable metal acupuncture needles of 0.25 mm in diameter and 40 mm in length were used. The areas of acupoints were sterilized with alcohol swabs before the insertion of needles. The needles were inserted into the appropriate depth of each acupoint; however, De Qi sensation was not necessarily elicited. The needles stayed in without further manipulation for 30 minutes at each session before being removed.

Five days after the start of acupuncture treatments, the patient spontaneously reported "I slept much more (7.5-8.0 h on sleep diary) than normal and I stayed asleep after I fell asleep. One night I didn't need medication." At the end of the 8-week treatment course, the patient continued to report "falling asleep easier" and "staying asleep longer." She had another 2 days of post-treatment actigraphy monitoring. During those 2 nights, she used no medication to assist with sleep. On sleep diary, she reported the first night being fragmented due to "great deal of pain in my knees," and the second night still characterized by "some knee pain." Her mean sleep duration for these 2 nights was estimated at 7 hours. Her PSQI score decreased to 8, and her GDS decreased to 19. Wrist actigraph recording showed 2-night average SE 76.7%, TST 490 minutes, and WASO 136 minutes. Her health-related quality of life (HRQoL) using Medical Outcomes Study 36-item Acute Form (SF-36 Acute)[128] showed the most substantial improvement in the subscales of role limitations due to physical health and social functioning (improvement of 50 points each on a 100-point scale), also improvements in vitality (10 points), emotional well-being (32 points), and general health (10 points). Finally, the use of lorazepam was reported to decrease from daily to once a week over a period of 12 weeks followed.

Case #2

A 50-year-old African American male combat veteran presented with chronic insomnia and polytrauma, including a moderate traumatic brain injury (TBI) due to a blast injury in 2008 with concomitant severe headaches afterwards, as well as right elbow and forearm injuries in a rocket-propelled grenade attack in 2004, status post 13 surgeries to repair the damages sustained. He had a fixed right elbow with pain and significant amount of lymphedema requiring compressive dressing all the time. Other medical conditions included allergic rhinitis, gastroesophageal reflux disease, and hypertension.

At his initial presentation, his PSQI score was 11, with 5 h of sleep per night on average, and habitual sleep efficiency of 63%. His Modified Post-Traumatic Stress Disease (PTSD) Symptoms Scale Self-Report (MPSS-SR) was 20 (Range: 0-51 on 17 items, with higher score representing worse symptoms).[129] Headaches were 9/10 in intensity, with a frequency of 1-3 per week. He reported that the headaches "moderately" affected his work, life, and sleep.

Ten acupuncture treatments were performed during a five-and-half month period, at a frequency about once every 2 weeks. The acupuncture points were selected differently at different visits to treat mainly headaches, anxiety, and sleep, guided by Traditional Chinese Medicine meridian theories. Number of needles varied from 8 to 18.

After these treatments, the patient reported "overall" improvements. Headaches went down to 3/10 in intensity at a frequency of 1-2 per month. He reported that the headaches "moderately" affected his work, but "mildly" affected his life and sleep. His PTSD MPSS-SR scored 15. His PSQI score was also improved to 8, with 6 h of sleep per night on average, and habitual sleep efficiency of 75%. The patient rated the effectiveness of acupuncture in helping his conditions as 5.0 on a visual analog scale from 0 to 10.

Case #3

A 47-year-old African American female veteran presented with chronic insomnia, and prolonged PTSD symptoms after military service, with an initial MPSS-SR score of 40 out of 51. Her initial PSQI was 18. She also complained of severe headaches twice weekly at 10/10 level lasting average of 72 h, along with regular "daily" headaches at 4/10 level for over 18 years. She was using lamotrigine and sumatriptan at the time of presentation. Other medical conditions included hypertension treated with medications, myofascial pain syndrome, and degenerative joint problems with pain over 5 body parts (left shoulder, right elbow, mid-back, low-back, and knees), treated with trigger point injections and topical cream.

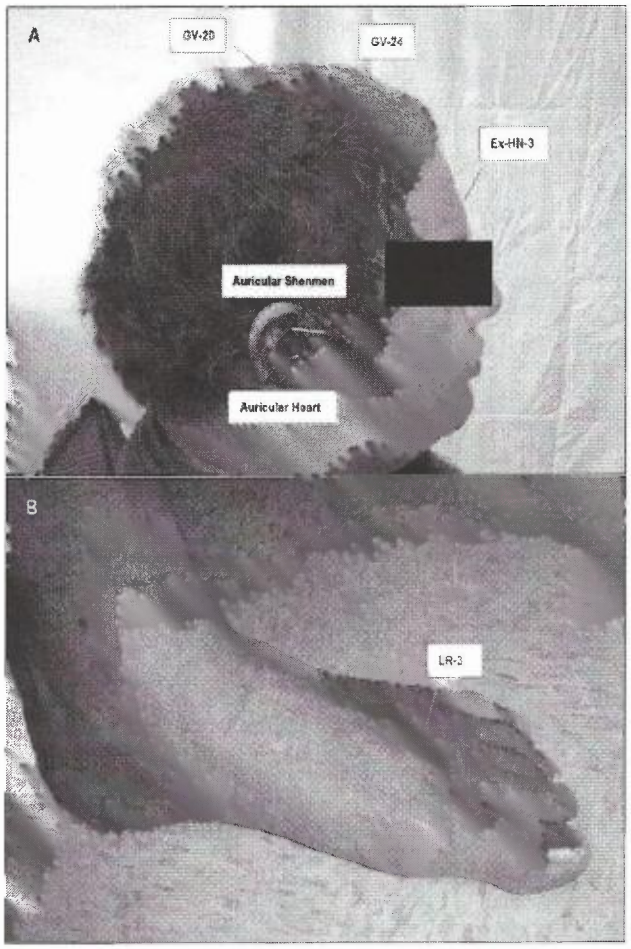
Ten acupuncture treatments were performed during 5 months, at a frequency about once every 2 weeks. The acupuncture points were selected differently at different visits to treat mainly anxiety, headaches, and sleep, guided by Traditional Chinese Medicine meridian theories and auricular mapping. Number of needles varied from 10 to 20. Both body and auricular points were used alone or in combination.

After these treatments, the patient's PTSD MPSS-SR score was reduced to 22. Her headaches were completely resolved after 6 treatments. She discontinued all headache medications with no rebound at follow-up 4 months after the end of last treatment. Her PSQI score also improved to 13, with sleep duration increased from 3 h per night on average to 4 h, and habitual sleep efficiency improved from 27% to 40%. She decreased the use of sleep medication (zolpidem 10 mg) from "three or more times a week" to "once or twice a week." The patient rated the effectiveness of acupuncture in helping her conditions as 9.5 on a visual analog scale from 0 to 10.

Discussion of Cases

These three cases represented a diverse sample of patients with chronic insomnia: a middle-aged patient with osteoarthritic knee pain, a middle-aged veteran with polytrauma, and a younger veteran with PTSD, who reported chronic disturbance in sleep. However, these three cases were selected also by a common theme—having comorbid insomnia and clinical manifestations of hyperarousal, e.g. PTSD or anxiety, and hypertension.

Figure 1—Demonstration of some commonly used acupuncture points for improving sleep



Acupuncture points were tailored for patient's specific conditions, with certain points frequently used in the treatments, such as Ex-HN-3 (Yintang), GV-24 (Shenting), GV-20 (Baihui), PC-6 (Neiguan), LR-3 (Taichong), auricular Shenmen, or auricular Heart. These points were mainly chosen for their sedating effects to treat anxiety/PTSD and sleep complaints, although some often assist in headache treatments, such as Ex-HN-3 (Yintang), GV-20 (Baihui) or LR-3 (Taichong). **Figure 1A** and **1B** are illustration of acupuncture at some of these points in a model.

The clinical success observed after acupuncture treatments in our patients included sleep improvements, such as prolonged sleep duration and increased sleep efficiency, anxiety symptom improvement, headache improvement/resolution, functional improvement, and/or less medication intake. Because this was a preliminary clinical case series, objective measurements of sleep outcome were not widely used, nor were measurements of autonomic activities included. Thus, the interpretation of

these results remains clinical rather than mechanistic. We use these cases to illustrate the need for such future sleep research to complement the clinical findings and, in turn, to better guide future clinical practice.

FUTURE CONSIDERATIONS

As we have reviewed here and elsewhere, many studies have documented physiological effects of acupuncture using the standards of contemporary Western science. In all likelihood some of those improvements are mediated by autonomic activities. Our cases further illustrate that acupuncture may have substantial and dramatic effects in patients who report substantially disturbed sleep. Future clinical trials employing both site- and stimulation-specific controls should be undertaken to attest that this ancient medical practice may have impact on sleep. Monitoring autonomic activation may represent a novel attempt both to understand how acupuncture works and to assess current mediational models for insomnia.

REFERENCES

1. Huang W, Kutner N, Bliwise DL. A systematic review of the effects of acupuncture in treating insomnia. *Sleep Med Rev* 2009;13:73-104.
2. Richardson GS. Human physiological models of insomnia. *Sleep Med* 2007;8(Suppl. 4):S9-S14.
3. Roth T, Roehrs T, Pies R, et al. Insomnia: pathophysiology and implications for treatment. *Sleep Med Rev* 2007;11:71-9.
4. Bonnet M, Arand D. Hyperarousal and insomnia. *Sleep Med Rev* 1997;1:97-108.
5. Stepanski E, Zorick F, Roehrs T, et al. Daytime alertness in patients with chronic insomnia compared with asymptomatic control subjects. *Sleep* 1988;11:54-60.
6. Bonnet MH, Arand DL. 24-Hour metabolic rate in insomniacs and matched normal sleepers. *Sleep* 1995;18:581-88.
7. Seidel WF, Ball S, Cohen S, et al. Daytime alertness in relation to mood, performance, and nocturnal sleep in chronic insomniacs and noncomplaining sleepers. *Sleep* 1984;7:230-8.
8. Merica H, Gaillard JM. The EEG of the sleep onset period in insomnia: a discriminant analysis. *Physiol Behav* 1992;52:199-204.
9. Perlis ML, Smith MT, Andrews PJ, et al. Beta/Gamma EEG activity in patients with primary and secondary insomnia and good sleeper controls. *Sleep* 2001;24:110-7.
10. Krystal AD, Edinger JD, Wohlgemuth WK, et al. NREM sleep EEG frequency spectral correlates of sleep complaints in primary insomnia subtypes. *Sleep* 2002;25:630-40.
11. Hall M, Thayer JF, Germain A, et al. Psychological stress is associated with heightened physiological arousal during NREM sleep in primary insomnia. *Behav Sleep Med* 2007;5:178-93.
12. Drake C, Richardson GS, Roehrs T, et al. Vulnerability to stress-related sleep disturbance and hyperarousal. *Sleep* 2004;27:285-91.
13. Smith MT, Perlis ML, Chengazi VU, et al. Neuroimaging of NREM sleep in primary insomnia: a Tc-99-HMPAO single photon emission computed tomography study. *Sleep* 2002;25:325-35.
14. Nofzinger EA, Buysse DJ, Germain A, et al. Functional neuroimaging evidence for hyperarousal in insomnia. *Am J Psychiatry* 2004;161:2126-8.
15. Winkelman JW, Buxton OM, Jensen JE, et al. Reduced brain GABA in primary insomnia: preliminary data from 4T proton magnetic resonance spectroscopy (1H-MRS). *Sleep* 2008;31:1499-506.
16. Lushington K, Dawson D, Lack L. Core body temperature is elevated during constant wakefulness in elderly poor sleepers. *Sleep* 2000;23:504-10.
17. Monroe LJ. Psychological and physiological differences between good and poor sleepers. *J Abnorm Psychol* 1967;72:255-64.
18. Freedman RR, Sattler HL. Physiological and psychological factors in sleep-onset insomnia. *J Abnorm Psychol* 1982;91:380-9.
19. Broman J, Hetta J. Electrodermal activity in patients with persistent insomnia. *J Sleep Res* 1994;3:165-70.
20. Bonnet MH, Arand DL. Heart rate variability in insomniacs and matched normal sleepers. *Psychosom Med* 1998;60:610-15.
21. Vgontzas AN, Bixler EO, Lin HM, et al. Chronic insomnia is associated with nyctohemeral activation of the hypothalamic-pituitary-adrenal axis: Clinical implications. *J Clin Endocrinol Metab* 2001;86:3787-94.
22. Chang FC, Opp MR. Corticotropin-releasing hormone (CRH) as a regulator of waking. *Neurosci Biobehav Rev* 2001;25:445-53.
23. Sugiyama Y, Xue YX, Mano T. Transient increase in human muscle sympathetic nerve activity during manual acupuncture. *Jpn J Physiol* 1995;45:337-45.
24. Tam KC, Yiu HH. The effect of acupuncture on essential hypertension. *Am J Chin Med* 1975;3:369-75.
25. Williams T, Mueller K, Cornwall MW. Effect of acupuncture-point stimulation on diastolic blood pressure in hypertensive subjects. *Phys Ther* 1991;71:523-9.
26. Ohsawa H, Yamaguchi S, Ishimaru H, et al. Neural mechanism of pupillary dilation elicited by electro-acupuncture stimulation in anesthetized rats. *J Auton Nerv Syst* 1997;64:101-6.
27. Hsu CC, Weng CS, Liu TS, et al. Effects of electrical acupuncture on acupoint BL15 evaluated in terms of heart rate variability, pulse rate variability and skin conductance response. *Am J Chin Med* 2006;34:23-36.
28. Ernst M, Lee MHM. Sympathetic vasomotor changes induced by manual and electrical acupuncture of the Hoku point visualized by thermography. *Pain* 1985;21:25-33.
29. Hsieh CL, Lin JG, Li TC, et al. Changes of pulse rate and skin temperature evoked by electroacupuncture stimulation with different frequency on both Zusanli acupoints in humans. *Am J Chin Med* 1999;27:11-8.
30. Knardahl S, Elam M, Olausson B, et al. Sympathetic nerve activity after acupuncture in humans. *Pain* 1998;75:19-25.
31. Nishijo K, Mori H, Yosikawa K, et al. Decreased heart rate by acupuncture stimulation in humans via facilitation of cardiac vagal activity and suppression of cardiac sympathetic nerve. *Neurosci Lett* 1997;227:165-8.
32. Haker E, Egekvist H, Bjerring P. Effect of sensory stimulation (acupuncture) on sympathetic and parasympathetic activities in healthy subjects. *J Auton Nerv Syst* 2000;79:52-9.
33. Li ZY, Jiao K, Chen M, et al. Effect of magnitopuncture on sympathetic and parasympathetic nerve activities in healthy drivers - assessment by power spectrum analysis of heart rate variability. *Eur J Appl Physiol* 2003;88:404-10.
34. Litscher G. Bioengineering assessment of acupuncture, Part 7: heart rate variability. *Crit Rev Biomed Eng* 2007;35:183-95.
35. Andersson S, Lundeberg T. Acupuncture - from empiricism to science: functional background to acupuncture effects in pain and disease. *Med Hypotheses* 1995;45:271-81.
36. Ernst M, Lee MHM. Sympathetic effects of manual and electrical acupuncture of the Tsusanli knee point: comparison with the Hoku hand point sympathetic effects. *Exp Neurol* 1986;94:1-10.
37. Tjen-A-Looi SC, Li P, Longhurst JC. Medullary substrate and differential cardiovascular responses during stimulation of specific acupoints. *Am J Physiol Regul Integr Comp Physiol* 2004;287:R852-62.
38. Chae Y, Park HJ, Koo ST, et al. Review on acupuncture and autonomic nervous system: heart rate variability analysis in humans. *J Meridian Acupoint* 2007;24:25-36.
39. Wang JD, Kuo TBJ, Yang CCH. An alternative method to enhance vagal activities and suppress sympathetic activities in humans. *Auton Neurosci* 2002;100:90-5.
40. Lewith GT, Machin D. On the evaluation of clinical effects of acupuncture. *Pain* 1983;16:111-27.
41. Ballegaard S, Muteki T, Harada H, et al. Modulatory effect of acupuncture on the cardiovascular system: a cross-over study. *Acupunct Electrother Res* 1993;18:103-15.
42. Syuu Y, Matsubara H, Kiyooka T, et al. Cardiovascular beneficial effects of electroacupuncture at Neiguan (PC-6) acupoint in anesthetized open-chest dog. *Jpn J Physiol* 2001;51:231-8.
43. Rutkowski B. Electrical stimulation and essential hypertension. *Acupunct Electrother Res* 1980;5:287-95.
44. Andersson S. The functional background in acupuncture effects. *Scand J Rehabil Med Suppl* 1993;29:31-60.
45. Omura Y. Patho-physiology of acupuncture treatment: effects of acupuncture on cardiovascular and nervous systems. *Acupunct Electrother Res Int J* 1975;1:51-140.
46. Smith FWJ. Acupuncture for cardiovascular disorders. *Probl Vet Med* 1992;4:125-31.
47. VanWormer AM, Lindquist R, Sendelbach SE. The effects of acupuncture on cardiac arrhythmias: a literature review. *Heart Lung* 2008;37:425-31.
48. Li P, Huangfu DH, Guo XQ, et al. [Role of the ventrolateral medullary area in the inhibitory effect of electroacupuncture on experimental pressor response and arrhythmia] (Chinese). *Zhen Ci Yan Jiu* 1986;11:166-73.

49. Xia Y, Guo XQ, Zhang AZ, et al. Inhibitory effect of analogous electro-acupuncture on experimental arrhythmia. *Acupunct Electrother Res* 1985;10:13-34.
50. Guo HF, Tian J, Wang X, et al. Brain substrates activated by electroacupuncture of different frequencies (I): Comparative study on the expression of oncogene c-fos and genes coding for three opioid peptides. *Brain Res Mol Brain Res* 1996;43:157-66.
51. Guo HF, Tian J, Wang X, et al. Brain substrates activated by electroacupuncture (EA) of different frequencies (II): Role of Fos/Jun proteins in EA-induced transcription of preproenkephalin and preprodynorphin genes. *Brain Res Mol Brain Res* 1996;43:167-73.
52. Han J-S, Terenius L. Neurochemical basis of acupuncture analgesia. *Annu Rev Pharmacol Toxicol* 1982;22:193-220.
53. Han JS. Electroacupuncture: an alternative to antidepressants for treating affective diseases. *Int J Neurosci* 1986;29:79-92.
54. Malizia E, Andreucci G, Paolucci D, et al. Electroacupuncture and peripheral beta-endorphin and ACTH levels. *Lancet* 1979;2:535-6.
55. Schneider A, Weiland C, Enck P, et al. Neuroendocrinological effects of acupuncture treatment in patients with irritable bowel syndrome. *Complement Ther Med* 2007;15:255-63.
56. Akimoto T, Nakahori C, Aizawa K, et al. Acupuncture and responses of immunologic and endocrine markers during competition. *Med Sci Sports Exerc* 2003;35:1296-302.
57. He L, Xu S. Caudate nucleus and acupuncture analgesia. *Acupunct Electrother Res* 1981;6:169-82.
58. Baek YH, Choi DY, Yang HI, et al. Analgesic effect of electroacupuncture on inflammatory pain in the rat model of collagen-induced arthritis: mediation by cholinergic and serotonergic receptors. *Brain Res* 2005;1057:181-5.
59. Spence DW, Kayumov L, Chen A, et al. Acupuncture increases nocturnal melatonin secretion and reduces insomnia and anxiety: a preliminary report. *J Neuropsychiatry Clin Neurosci* 2004;16:19-28.
60. Bucinskaite V, Theodorsson E, Crumpton K, et al. Effects of repeated sensory stimulation (electro-acupuncture) and physical exercise (running) on open-field behaviour and concentrations of neuropeptides in the hippocampus in WKY and SHR rats. *Eur J Neurosci* 1996;8:382-7.
61. Bucinskaite V, Lundeberg T, Stenfors C, et al. Effects of electro-acupuncture and physical exercise on regional concentrations of neuropeptides in rat brain. *Brain Res* 1994;666:128-32.
62. Kim E-H, Jang M-H, Shin M-C, et al. Acupuncture increases cell proliferation and neuropeptide Y expression in dentate gyrus of streptozotocin-induced diabetic rats. *Neurosci Lett* 2002;327:33-6.
63. Gan P, Cheng JS, Ng YK, et al. Role of GABA in electro-acupuncture therapy on cerebral ischemia induced by occlusion of the middle cerebral artery in rats. *Neurosci Lett* 2005;383:317-21.
64. Lee BH, Zhao RJ, Moon JY, et al. Differential involvement of GABA system in mediating behavioral and neurochemical effect of acupuncture in ethanol-withdrawn rats. *Neurosci Lett* 2008;443:213-7.
65. Shu J, Liu RY, Huang XF, et al. The effects of ear-point stimulation on the contents of somatostatin and amino acid neurotransmitters in brain of rat with experimental seizure. *Acupunct Electrother Res* 2004;29:43-51.
66. Zhao P, Huang ZN, Chen G, et al. Electro-acupuncture attenuates nitric oxide release from rat striatum after transient middle cerebral artery occlusion. *Acupunct Electrother Res* 2000;25:101-7.
67. Zhai D, Din B, Liu R, et al. [Regulation on ACTH, beta-EP and immune function by moxibustion on different acupoints] (Chinese). *Zhen Ci Yan Jiu* 1996;21:77-81.
68. Wen HL, Ho WK, Wong HK, et al. Reduction of adrenocorticotropic hormone (ACTH) and cortisol in drug addicts treated by acupuncture and electrical stimulation (AES). *Comp Med East West* 1978;6:61-6.
69. Nunley C, Wakim J, Guinn C, et al. The effects of stimulation of acupressure point p6 on postoperative nausea and vomiting: a review of literature. *J Perianesth Nurs* 2008;23:247-61.
70. Guo ZL, Moazzami AR, Tjen ALS, et al. Responses of opioid and serotonin containing medullary raphe neurons to electroacupuncture. *Brain Res* 2008;1229:125-36.
71. Yuan Q, Li JN, Liu B, et al. Effect of Jin-3-needling therapy on plasma corticosteroid, adrenocorticotrophic hormone and platelet 5-HT levels in patients with generalized anxiety disorder. *Chin J Integr Med* 2007;13:264-8.
72. Zhu Y, Liu QY, Zhuo LS, et al. [Influence of electroacupuncture of "Baihui" (GV 20) and "Sanyinjiao" (SP 6) on hippocampal 5-HT and AChE immuno-activity in chronic depression rats] (Chinese). *Zhen Ci Yan Jiu* 2009;34:16-20.
73. Guan X, Liang X, Liu X. [Acetylcholine and the primary input of acupuncture sensation--influence of peripheral acetylcholine on the role of electroacupuncture analgesia] (Chinese). *Zhen Ci Yan Jiu* 1990;15:136-9.
74. Guan X, Wang C, Yu B, et al. [Research on the relationship between central acetylcholine and acupuncture analgesia] (Chinese). *Zhen Ci Yan Jiu* 1991;16:129-37.
75. Uchida S, Kagitani F, Suzuki A, et al. Effect of acupuncture-like stimulation on cortical cerebral blood flow in anesthetized rats. *Jpn J Physiol* 2000;50:495-507.
76. Sun AY, Boney F, Lee DZ. Electroacupuncture alters catecholamines in brain regions of rats. *Neurochem Res* 1985;10:251-8.
77. Zhou Y, Wang Y, Fang Z, et al. [Influence of acupuncture on blood pressure, contents of NE, DA and 5-HT of SHR and the interrelation between blood pressure and whole blood viscosity] (Chinese). *Zhen Ci Yan Jiu* 1995;20:55-61.
78. Wang Y, Wang S, Zhang W. Effects of naloxone on the changes of pain threshold and contents of monoamine neurotransmitters in rat brain induced by EA. *J Tradit Chin Med* 1991;11:286-90.
79. Gan P, Cheng JS, Ng YK, et al. Role of GABA in electro-acupuncture therapy on cerebral ischemia induced by occlusion of the middle cerebral artery in rats. *Neurosci Lett* 2005;383:317-21.
80. Lee BH, Zhao RJ, Moon JY, et al. Differential involvement of GABA system in mediating behavioral and neurochemical effect of acupuncture in ethanol-withdrawn rats. *Neurosci Lett* 2008;443:213-7.
81. Danjou P, Puech A, Warot D, et al. Lack of sleep-inducing properties of propranolol (80 mg) in chronic insomniacs previously treated by common hypnotic medications. *Int Clin Psychopharmacol* 1987;2:135-40.
82. Rosen R, Kostis J. Biobehavioral sequellae associated with adrenergic-inhibiting antihypertensive agents: a critical review. *Health Psychol* 1985;4:579-604.
83. Kostis J, Rosen R, Holzer B, et al. CNS side effects of centrally-active antihypertensive agents: a prospective, placebo-controlled study of sleep, mood state, and cognitive and sexual function in hypertensive males. *Psychopharmacology* 1990;102:163-70.
84. Astin JA. Why patients use alternative medicine: results of a national study. *JAMA* 1998;279:1548-53.
85. Mayer DJ. Antagonism of acupuncture analgesia in man by the narcotic antagonist naloxone. *Brain Res* 1977;121:368-72.
86. Galetti R, Procacci PC. The role of the sympathetic nervous system in the control of somatic pain and associated phenomena. *Acta Neuroveg* 1966;28:495-500.
87. Akil H, Watson SJ, Young E, et al. Endogenous opioids: biology and function. *Annu Rev Neurosci* 1984;7:223-55.
88. Bäcker M, Grossman P, Schneiner J, et al. Acupuncture in migraine - investigation of autonomic effects. *Clin J Pain* 2008;24:106-15.
89. Virsik, Kristufek P, Bangha O, et al. The effect of acupuncture on pulmonary function in bronchial asthma. *Prog Respir Res* 1980;14:271-5.
90. Kavoussi B, Ross BE. The neuroimmune basis of anti-inflammatory acupuncture. *Integr Cancer Ther* 2007;6:251-7.
91. Benenson EV, Dribina OG. [Clinical effectiveness and mechanism of action of auricular electroacupuncture in rheumatoid arthritis] (Russian). *Ter Arkh* 1981;53:42-6.
92. Moon P-D, Jeong H-J, Kim S-J et al. Use of electroacupuncture at ST36 to inhibit anaphylactic and inflammatory reaction in mice. *Neuroimmunomodulation* 2007;14:24-31.
93. Dundee JW, McMillan CM. Clinical uses of P6 acupuncture antiemesis. *Acupunct Electrother Res* 1990;15:211-5.
94. Dundee JW, McMillan C. Positive evidence for P6 acupuncture antiemesis. *Postgrad Med J* 1991;67:417-22.
95. Takahashi T. Acupuncture for functional gastrointestinal disorders. *J Gastroenterol* 2006;41:408-17.
96. Lin X, Liang J, Ren J, et al. Electrical stimulation of acupuncture points enhances gastric myoelectrical activity in humans. *Am J Gastroenterol* 1997;92:1527-30.
97. Berman AH, Lundberg U, Krook AL, et al. Treating drug using prison inmates with auricular acupuncture: a randomized controlled trial. *J Subst Abuse Treat* 2004;26:95-102.
98. Bernstein KS. The experience of acupuncture for treatment of substance dependence. *J Nurs Scholarsh* 2000;32:267-72.
99. Janssen PA, Demorest LC, Whynot EM. Acupuncture for substance abuse treatment in the Downtown Eastside of Vancouver. *J Urban Health* 2005;82:285-95.
100. Hollifield M, Sinclair-Lian N, Warner TD, et al. Acupuncture for posttraumatic stress disorder: a randomized controlled pilot trial. *J Nerv Ment Dis* 2007;195:504-13.
101. Pilkington K, Kirkwood G, Rampes H, et al. Acupuncture for anxiety and anxiety disorders--a systematic literature review. *Acupunct Med* 2007;25:1-10.
102. Hoffmann P, Thoren P. Long-lasting cardiovascular depression induced by acupuncture-like stimulation of the sciatic nerve in unanaesthetized rats. Effects of arousal and type of hypertension. *Acta Physiol Scand* 1986;127:119-26.
103. Tandon M, Philip FT. Comparison of real and placebo acupuncture in histamine-induced asthma. A doulbe-blinded cross-over study. *Chest* 1989;96:102-5.

104. Yin S, Cao Y, Zhang J. Treatment of primary hypotension by electroacupuncture at Neiguan and Gongsun--a report of 100 cases. *J Tradit Chin Med* 2004;24:193.
105. Syuu Y, Matsubara H, Hosogi S, et al. Pressor effect of electroacupuncture on hemorrhagic hypotension. *Am J Physiol Regul Integr Comp Physiol* 2003;285:R1446-52.
106. Li Y, Tougas G, Chiverton SG, et al. The effect of acupuncture on gastrointestinal function and disorders. *Am J Gastroenterol* 1992;87:1372-81.
107. Pomeranz B, Chiu D. Naloxone blockade of acupuncture analgesia: endorphin implicated. *Life Sci* 1976;19:1757-62.
108. Akil H, Mayer DJ, Liebeskind JC. Antagonism of stimulation produced analgesia by naloxone, a narcotic antagonist. *Science* 1976;191:961-2.
109. Han J-S. Acupuncture and endorphins. *Neurosci Lett* 2004;361:258-61.
110. Sjölund BH, Ericksson M. Increased cerebrospinal fluid levels of endorphins after electroacupuncture. *Acta Physiol Scand* 1977;100:382-4.
111. Zhang AZ, Pan XP, Xu SF, et al. Endorphines and acupuncture analgesia. *Chin Med J* 1980;93:673-80.
112. Cheng CH, Yi PL, Lin JG, et al. Endogenous opiates in the nucleus tractus solitarius mediate electroacupuncture-induced sleep activities in rats. *Evid Based Complement Alternat Med* 2009 Sep 3. [Epub ahead of print].
113. Li A, Lao L, Wang Y, et al. Electroacupuncture activates corticotrophin-releasing hormone-containing neurons in the paraventricular nucleus of the hypothalammus to alleviate edema in a rat model of inflammation. *BMC Complement Altern Med* 2008;8:20.
114. Wen HL, Cheung SYC. Reduction of adrenocorticotropic hormone (ACTH) and cortisol in drug addicts treated by acupuncture and electrical stimulation (AES). *Comp Med East West* 1978;6:61-6.
115. Liu S, Zhou W, Ruan X, et al. Activation of the hypothalamus characterizes the response to acupuncture stimulation in heroin addicts. *Neurosci Lett* 2007;421:203-8.
116. Chao D, Chen G, Cheng J. Melatonin might be one possible medium of electroacupuncture anti-seizures. *Acupunct Electrother Res* 2001;26:39-48.
117. Nordio M, Romanelli F. Efficacy of wrists overnight compression (HT 7 point) on insomniacs: possible role of melatonin? *Minerva Med* 2008;99:539-47.
118. Lewith GT, Kenyon JN. Physiological and psychological explanations for the mechanism of acupuncture as a treatment for chronic pain. *Soc Sci Med* 1984;19:1367-78.
119. Jessell TM, Iversen LL. Opiate analgesics inhibit substance P release from rat trigeminal nucleus. *Nature* 1977;268:549-51.
120. Zijlstra FJ, van den Berg-de Lange I, Huygen FJPM, et al. Anti-inflammatory actions of acupuncture. *Mediators Inflamm* 2003;12:59-69.
121. Feng JT, Hu CP, Li XZ. Dorsal root ganglion: the target of acupuncture in the treatment of asthma. *Adv Ther* 2007;24:598-602.
122. Fu LW, Longhurst JC. Electroacupuncture modulates vlPAG release of GABA through presynaptic cannabinoid CB1 receptors. *J Appl Physiol* 2009;106:1800-9.
123. Gao X, Ma Q, Hu B. Effects of acupuncture at Sishencong, EX-HN1. *Zhongguo Zhen Jiu* 2007;27:681-3.
124. Li S, Chen K, Wu Y, et al. Effects of warm needling at zusanli (ST 36) on NO and IL-2 levels in the middle-aged and old people. *J Tradit Chin Med* 2003;23:127-8.
125. Yeung W-F, Chung K-F, Zhang S-P, et al. Electroacupuncture for primary insomnia: a randomized controlled trial. *Sleep* 2009;32:1039-47.
126. Yesavage JA, Brink TL, Rose TL, et al. Development and validation of a geriatric depression screening scale: a preliminary report. *J Psychiatr Res* 1982;17:37-49.
127. World Health Organization. *Standard Acupuncture Nomenclature, 2nd ed.* World Health Orgainzation, 1993.
128. Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992;30:473-83.
129. Foa EB, Riggs DS, Dancu CV et al. Reliability and validity of a brief instrument for assessing posttraumatic stress disorder. *J Trauma Stress* 1993; 6:459-73.

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Address correspondence to: Donald Bliwise, Ph.D., Program in Sleep, Aging and Chronobiology, Emory University School of Medicine, Wesley Woods Health Center, 1841 Clifton Road, Room 509, Atlanta, GA 30329; Tel: (404) 728-4751; Fax: (404) 728-4756; E-mail: dbliwis@emory.edu

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