

SAR TURNING POINTS



When a White Horse is a Horse: Embracing the (Obvious?) Overlap Between Acupuncture and Neuromodulation

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Editor's Note: This column is another in our continuing series from the Society for Acupuncture Research (SAR). Vitaly Napadow, PhD, LAc, copresident of the SAR Board of Directors, is also the Director of the Center for Integrative Pain NeuroImaging (CiPNI) and associate professor at the Martinos Center for Biomedical Imaging at Massachusetts General Hospital, Harvard Medical School. In this commentary, Napadow expands on a theme engaged in 2016 *JACM* by SAR in an article entitled “Unanticipated Insights into Biomedicine from the Study of Acupuncture” (see his second reference). The exploration here is bidirectional—highlighting the rich intersection between electroacupuncture and that of neuromodulation device therapy, a relatively new growth area in modern biomedicine. —*John Weeks, Editor-in-Chief*



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THERE IS A WELL-KNOWN LOGIC PARADOX in Chinese philosophy dating back more than 2000 years that basically suggests that a white horse is not a horse due to the fact that a “white horse” is a member of two classes, both shape (i.e., horse) and color (i.e., white), while a “horse” is a member of only a single class: shape.¹ Thus, a white horse is certainly not identical to a horse. The ambiguity in the “white horse is a horse” paradox stems from whether the word “is” means “is a member of” or “is identical to.”

Although my goal here is not to attempt to definitively argue whether a white horse is, or is not, a horse, I do think that similar ambiguity exists between acupuncture and interventions encompassed by the broad class of “neuromodulation,” which is more broadly accepted by biomedical research and our healthcare system. Is acupuncture equivalent to neuromodulation, or vice versa? What can acupuncture researchers learn from neuromodulation research to better design and evaluate acupuncture therapies? Conversely, what can neuromodulation

device designers and researchers learn from the extensive research evidence base supporting acupuncture? Such cross-fertilization in research has been lacking, as touched upon by our previous review,² and should be better promoted.

In our current healthcare system, there is growing interest in nonpharmacological neuromodulation device-based therapies. Neuromodulation is an umbrella term for a class of interventions that act directly upon nerves, usually those of the peripheral nervous system. In fact, neuromodulation and electricity-based medical interventions have been around for hundreds of years,³ from electric eels to modern applications of transcutaneous electrical nerve stimulation (TENS) devices for pain control. Such interventions alter, or “modulate,” nerve activity by delivering electrical impulses directly to target nerves.

There is now growing interest by the biomedical and even pharmaceutical industry for more targeted electrical stimulation therapies, for both pain and nonpain indications. At the U.S. National Institutes of Health, the Common Fund’s Stimulating Peripheral Activity to Relieve Conditions (SPARC) is now focused on understanding nerve–organ interactions to ultimately advance the neuromodulation field toward precise treatment of diseases and conditions for which conventional therapies fall short.* In fact, a recent publication in *Nature* suggests that many neuromodulatory therapies can be considered “electroceuticals,” or in other words medicines that use electrical impulses (as opposed to pharmacological agents, as in “pharmaceuticals”) to modulate body physiology.⁴

Interestingly, many neuromodulatory therapies target cutaneously accessible peripheral nerves and receptors. In turn, acupuncture in general, and electroacupuncture in particular, which couples metallic (conductive) needles with electrical stimulation,⁵ significantly overlap with many new technologies falling under this broad neuromodulation umbrella. For instance, researchers have even referred to certain forms of TENS as “acupuncture-like” TENS, when using low-frequency stimulation, acupoint targeting, etc.⁶ Moreover, electroacupuncture and TENS may be modulating similar anatomical targets.⁷ The wealth of research already published covering neuromodulation and electroacupuncture therapy needs to be better integrated to further our understanding of mechanisms supporting these therapies. My contention is that both of these fields have quite a bit to learn from one another. Turning a blind eye to the (obvious) links threatens to retard potentially valuable advances in our understanding of how best to optimize promising directions in peripheral nerve stimulation therapies.

In fact, multiple examples of overlap or potential overlap between neuromodulation and electroacupuncture exist, both in concept and in practice. For instance, electrical stimulation applied to the median nerve, which tracks the pericardium (PC) meridian within the forearm, has been shown to modulate essential tremor⁸ and induce cardioprotective effects in animal models (e.g., reduced atrial remodeling⁹ and reduced ventricular arrhythmia¹⁰). Similarly, electroacupuncture applied over the PC meridian has been shown in a series of studies to reduce hypertension.¹¹ In fact, the overlap between median nerve neuromodulation and PC acupoint-targeted electroacupuncture was recently acknowledged in a review on device applications for cardiac outcomes.¹² Particularly near the wrist, the median nerve is quite shallow (~1 cm deep

from the skin surface) and easily accessible by an acupuncture needle. Hence electroacupuncture can be readily applied for median nerve neuromodulation, and locally targeted indications, such as carpal tunnel syndrome, respond well to electroacupuncture, with longitudinal improvements in median nerve function and brain neuroplasticity.¹³

Another important point is that cutaneous neuromodulation is noninvasive, leading to reduced barriers for entry by medical device companies. Several companies have now developed therapeutic devices targeting median nerve stimulation for various indications, including hypertension (e.g., eCoin, by Valencia Technologies, an example of a subcutaneous implanted neurostimulation device). Similarly, percutaneous tibial nerve stimulation has been applied by interventional urologists for many years for overactive bladder.^{14,15} This cutaneous neuromodulatory technique can target a region close to acupoint SP-6 on the medial aspect of the lower leg, and a recent review of electroacupuncture for overactive bladder synthesized data from 10 randomized controlled trials, finding support for reduced nocturia and improved quality of life.¹⁶

Another interesting example of overlap between cutaneous neuromodulation and acupuncture is with auricular transcutaneous vagus nerve stimulation,¹⁷ which has been shown to modulate function in several visceral organs (e.g., cardiac¹⁸ and gastrointestinal¹⁹ physiology) and typically targets a region of the auricle (e.g., cymba and cavum concha) that is thought to map to visceral organs such as the heart and gut in auricular acupuncture theory.²⁰ Stimulation of this region has been shown²¹ to activate nuclei (i.e., nucleus tractus solitarius) containing the primary brainstem synapse for the vagus nerve, whose efferent fibers are known to innervate the heart and the gut. Even more interestingly, such brainstem activation was found to be greater when stimulation occurs during the exhalatory phase of the respiratory cycle,²¹ possibly supporting the Chinese medicine concept of the importance of respiratory phase for acupuncture needle insertion to achieve tonification and dispersion, potentially having distinct effects on organ physiology.

Clearly, there is significant overlap in both practice and theory supporting acupuncture and neuromodulation. There have been a number of interesting innovations in neuromodulation that should be considered by acupuncturists, such as closed loop stimulation, flexibility in pulse waveforms, and implanted stimulators. Moreover, critical concepts promulgated in the neuromodulation field, such as “target engagement,” or the idea that a quantitative outcome metric can confirm that a physiological “target” of stimulation is actually modulated, could be important to translate to acupuncture research and/or clinical practice. In turn, acupuncture scholars and researchers have accumulated both empirical and research support for the safety, efficacy, and mechanisms of cutaneous or percutaneous stimulation to address multiple medical disorders—a knowledge base in need of greater consideration by a broader array of biomedical researchers and our healthcare system.

In summary, whether acupuncture is a form of neuromodulation may be simply asking whether a “white horse” is a “horse” in the ancient Chinese white horse paradox. For this example, the white horse may indeed be a horse, and we should embrace this overlap to further research in both fields, rather than turning a blind eye and needing to reinvent the wheel in research design and evaluation of both acupuncture and neuromodulation therapies.

*(<https://commonfund.nih.gov/sparc>).

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