Transdermal Electrical Neurostimulation Therapies in Psychiatry: A Review of the Evidence

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ABSTRACT

Electric current has been used for quite some time in the treatment of mental illness; however, less-invasive user-controlled transcranial electrical neurostimulation (TEN) devices have begun to enter the market. Developers claim significant positive effects across a variety of physical and mental illnesses, as well as more mundane issues of stress and fatigue. However, the field is young and progressing rapidly, and no review of these claims has been conducted to date. This article summarizes the available evidence for user-controlled TEN devices, divided into three domains: efficacy/effectiveness, usability/safety, and mechanics. Limitations in the existing research base are noted and suggestions for future investigation are provided. [Psychiatr Ann. 2016;46(10):589-593.]

The use of electric current to treat psychiatric conditions has a long history. For example, electroconvulsive treatment (ECT) has been in clinical use since 1938. Despite repeated demonstrations of the efficacy and overall safety of ECT, its use is limited due to the invasive nature of the treatment and the potential for side effects.1 More recently, transcranial direct current stimulation (tDCS), which directs current to certain localized brain areas without induction of seizures, has been studied for psychiatric disorders.2 Finally, several techniques have recently been developed that patients can deliver to themselves, and that propose to deliver weak current to superficial cranial nerve sites as a treatment for psychiatric disorders. These techniques have been called by various names including: transdermal electrical neurostimulation (TEN), transdermal electrical stimulation, and cranial...
electrical stimulation. However, as with many developing interventions, the supporting empirical literature regarding the efficacy of these techniques is relatively sparse. This review surveys this literature, commenting on the current state of the field and suggests avenues for further research. Devices included in this review were those that claim to directly address discrete mental health conditions and can be used without the guidance of a trained professional.

Three TEN devices were identified that met the above inclusion criteria: Thync (Thync, Inc; Boston, MA), Alpha-Stim (Electromedical Products International, Inc; Mineral Wells, TX), and the Fisher Wallace Stimulator (Fisher Wallace Laboratories; New York, NY). Each device manufacturer has made specific claims about their products’ potential for improving mental health conditions or psychological well-being, and each device can be applied by patients with minimal risk or training. These user-controlled products differ significantly from more invasive electrical stimulation techniques that require supervision from medical professionals; rather user-controlled techniques rely on preprogrammed stimulation routines with fewer options for customization by the user.

User-administered devices that deliver electrical stimulation are also often seen as part of the “new field” of wearable technologies. Devices in this category are frequently not regulated at a level comparable to that for more invasive medical devices; as a result, there is not a requirement for controlled clinical trials. Nevertheless, some efforts to study the efficacy, tolerability and safety, and mechanism of action of these devices have been undertaken. Several reviews and meta-analyses of professionally administered TEN treatments for psychiatric disorders report mixed results, but with some promising indications of effectiveness.

**TEN DEVICES—THE CURRENT EVIDENCE BASE**

**Efficacy/Effectiveness**

The most recently released device, Thync, is somewhat of an outlier in the field because it is marketed almost exclusively to people without significant mental health struggles as a means of increasing alertness/focus or decreasing subjective stress. Promisingly, the developers have been able to demonstrate moderate positive effects in these domains. An innovative study conducted by several of the developers tested whether use of the Thync device would suppress a number of biological markers of sympathetic nervous system activation and distress (skin surface temperature measured by infrared emission; subjective “tension and anxiety” measured by survey; heart rate; galvanic skin response; and salivary alpha-amylase concentration) in both the resting-state and induced-stress conditions. Their findings indicated that all markers of increased activation of the sympathetic system were suppressed in people that used Thync in both conditions. Another study conducted by the developers found that regular use of Thync prior to sleep improved subjective sleep quality and mood, based on self-report survey results (Positive and Negative Affect Schedule and Depression and Anxiety Stress Scales) and actigraphy measurements. As the Thync device continues to mature, it will be of interest whether these positive results can be extended to clinical populations.

In comparison, the Alpha-Stim device has a larger and more diverse empirical base. A succession of randomized controlled trials has established some degree of efficacy for the device in syndromes as varied as fibromyalgia and insomnia, as well as a number of psychiatric conditions. Several open clinical trials and case studies have also yielded positive results. In terms of the effectiveness of the Alpha-Stim in treating psychiatric disorders, a study found that 5 weeks of treatment with an Alpha-Stim moderately reduced scores on the Hamilton Rating Scale for Anxiety and Hamilton Rating Scale for Depression in people with a primary anxiety disorder. Moderate reductions in depression-related scores on the Beck Depression Inventory (BDI) and the Brief Symptom Inventory were also found in a sample of sheriff’s officers. An open study of military service members and veterans found that, for those responding to the survey, the Alpha-Stim was effective in reducing subjective impairment resulting from generalized anxiety, posttraumatic stress disorder, insomnia, and depression. A pilot study of people with primary anxiety disorders also yielded positive results in the moderate range. Additionally, a retrospective study found mixed results in a cohort of patients with chronic bipolar disorder, in that Clinical Global Impressions scores improved significantly while having no reliable effect on mood symptoms. Finally, an older open study found positive effects of Alpha-Stim use in people with anxiety disorders.

The Fisher Wallace Stimulator has been applied to a wide range of physical illnesses. However, its effectiveness in the treatment of mental illness has been poorly studied. Only one extant publication could be located that specifically tested the Fisher Wallace Stimulator—a pilot study involving people with depressive symptoms in the context of bipolar II disorder found moderate but brief improvement in subjective symptom severity based on scores on the BDI.

**Usability/Safety**

One study simultaneously testing an unrelated tDCS device for comparison, found no adverse events in over 646 Thync treatment sessions by
30 healthy volunteers during a 6-week period. However, neither the Alpha-Stim nor the Fisher Wallace Stimulator have been specifically investigated for usability/safety in rigorous controlled research. Nonetheless, there is a large corpus of safety and usability literature that finds low-amperage tDCS and TEN devices to be well-tolerated by users.¹⁸

Mechanics
Researchers using Thync proposed that electrical stimulation of certain branches of the trigeminal and facial afferent nerves modulates a noradrenergic system extending from several nuclei in the extended reticular activating system into various regions in the thalamus and limbic system. This mechanism is postulated to affect arousal and cognition.³,¹⁰ Developers of Alpha-Stim posited that electrical stimulation of different branches of cranial afferent nerves modulates acetylcholinergic and serotonergic systems projecting via the raphe nucleus onto various thalamic nuclei. This pathway is described as having direct effects on mood, anxiety, and cognition.¹⁹ In contrast, investigators using the Fisher Wallace Stimulator have not suggested a specific method of action, either including mediating pathways via cranial nerves or by the transcranial passage of current into cortical and/or subcortical neuroanatomical structures.⁵,²⁰

LIMITATIONS OF THE CURRENT EVIDENCE BASE
As noted earlier, the existing research basis for TEN treatments as a whole, and specifically user-controlled TEN devices, shows a number of promising indications of effectiveness. However, the limitations of this literature are substantial. The number of studies directly investigating the user-controlled devices is extremely small, and the participant samples for those studies that have been conducted are themselves small, and often geographically restricted and not representative of the population being studied. Methodological problems abound, mechanisms for the selection and inclusion of participants in studies of the treatment of mental illness are troublingly heterogeneous, in our view, and follow-up times for clinical outcomes are almost universally short (e.g., 2-6 weeks). The range of psychiatric disorders assessed is also limited. Furthermore, the clinical-outcome literature suffers from a lack of investigation of long-term usage or repeated usage, so no conclusions can be drawn about the viability of user-controlled TEN treatment as an enduring treatment option. Alongside these limitations, most of the extant research was conducted by product developers or stakeholders, and the positive findings have not been replicated by independent practitioners. Even the larger corpus of research on TEN treatments as a whole possesses significant flaws, with De Felice⁵ concluding that “few of these trials can be considered to be rigorous and well-controlled according either to the criteria used by Klawansky et al. 1995 or by the US Food and Drug Administration.” These issues must be resolved before truly valid and reliable claims can be made about the efficacy and effectiveness of the user-controlled TEN devices.

In our view, another important problem with the field, as it stands, is the heterogeneity of the design of the user-controlled TEN devices. Thync involves a small battery pack placed on top of an electrode between the right eyebrow and hairline, with an additional electrode placed either behind the ear or on the back of the neck. In contrast, the Alpha-Stim device is applied via clips to both earlobes, whereas the Fisher Wallace Stimulator uses two electroconductive pads placed on opposite sides of the forehead and secured with a simple velcro headband. Thus, notwithstanding the similar hypotheses regarding the mechanics of the various devices, the existing literature has not yet produced a reliable empirical basis for these claims, and it is possible that differing mechanisms are responsible for the effects seen with each device.

Indeed, in many respects the design and implementation of TEN devices is constrained by the generally poor understanding of the mechanics of transdermal and transcranial electrical stimulation. According to Mondino et al.,¹⁸ commenting on the wider tDCS literature, “Parameters of stimulation are heterogeneous between studies, particularly in terms of current strength, number of sessions and delay between sessions.” They go on also to criticize the lack of consistency in electrode placement based on rudimentary and insufficiently understood models of the transmission of electrical current from the electrodes to the brain regions of interest. For example, many of the studies underpinning the user-controlled devices presuppose that current is carried along several branches of the trigeminal nerve into the brainstem, and thence upward into the thalamus and limbic system; at least one model, however, predicts that a substantial amount of current passes directly through the skull and into the underlying nervous tissue without mediation by the cranial nerves (however,
the prediction was not tested in a controlled study). These limitations in the fundamental understanding of the mechanics of TEN make it extremely difficult to design research protocols or new devices in such a way as to make them consistently and meaningfully comparable.

Despite these important methodological problems, several studies\(^ {6,7}\) were conducted to attempt to compare professionally administered TEN treatment with pharmacological treatment-as-usual. Brunoni et al.\(^ {4}\) compared the effectiveness of sertraline and tDCS in a factorial randomized controlled trial. Participants were people with nonpsychotic, unipolar major depressive disorder who were not taking medications at the time of the trial. The results indicated that the effectiveness of tDCS was similar to sertraline, but that combined treatment was the most effective. Interestingly, an additional exploratory analysis of the data found evidence that the clinical effects are the result of action along differing depression pathways.\(^ {22}\) A variety of other complicated pharmacological interactions have also been noted.\(^ {18}\) However, a follow-up study\(^ {23}\) noted that, although the tDCS treatments were safe, they were no more effective than sertraline for people with treatment-refractory depression. Thus, establishing the differential value of tDCS over treatments as usual, particularly in more complex cases involving refractory mental illnesses, may be a challenge for developers and researchers.

**DISCUSSION AND FUTURE DIRECTIONS**

User-controlled TEN devices reflect a new and growing niche within the field of transdermal/transcranial electrical stimulation, one that holds some promise of becoming a convenient and easily available treatment for mental illness. Proponents suggest that it is a safe and effective means of reducing symptom severity and functional impairment.\(^ {3,5,8,24}\) However, the empirical literature is still largely in its infancy, and many of the claims made by the developers of TEN devices are not firmly supported by the evidence. In our view, a convincing case had been made that a more comprehensive model of the underlying mechanism would help focus future development and provide a better foundation for any associated clinical claims. User-controlled TEN appears to be a promising but emergent intervention for mental health conditions, and producing a more robust empirical basis should be a top priority for developers and interested researchers looking for an innovative option for treatment.

**REFERENCES**

10. Boasso AM, Mortimore H, Silva R, Aven L, Tyler WJ. Transdermal electrical neuromodulation: a new and growing niche within the field of transdermal/transcranial electrical stimulation, one that holds some promise of becoming a convenient and easily available treatment for mental illness. Proponents suggest that it is a safe and effective means of reducing symptom severity and functional impairment. However, the empirical literature is still largely in its infancy, and many of the claims made by the developers of TEN devices are not firmly supported by the evidence. In our view, a convincing case had been made that a more comprehensive model of the underlying mechanism would help focus future development and provide a better foundation for any associated clinical claims. User-controlled TEN appears to be a promising but emergent intervention for mental health conditions, and producing a more robust empirical basis should be a top priority for developers and interested researchers looking for an innovative option for treatment.


