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Effectiveness of Vagus Nerve Stimulation by Auricular Acupuncture for Fear Extinction in PTSD – A Narrative Review

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ABSTRACT

Post-traumatic stress disorder (PTSD) is a response to trauma that results in a chronic perception of threat. These individuals can find themselves caught in reoccurring patterns of defensive reactions to neutral situations, with an inability to shift out of this fearful state. Comorbidities are frequent in patients with PTSD, and the chronic stress pathologies associated with PTSD is a critical health issue. Clinical care offers a low effectiveness rate, is often delayed, and many with PTSD still go untreated. The elimination (extinction) of this conditioned fear in PTSD requires the creation of new memories that compete with fearful connections, most often accomplished through exposure-based therapies. Current studies have determined that vagus nerve stimulation (VNS) can modulate the autonomic nervous system in a way that enhances the extinction of this conditioned fear in PTSD when used in conjunction with exposure-based therapies. Current research shows that acupuncture can also modulate the autonomic nervous system through VNS for treatments of blood pressure, insomnia, tinnitus, and other diseases. Furthermore, Acupuncture has been determined to be a safe, potentially non-stigmatizing treatment that can reduce the symptoms of, depression, anxiety, and chronic pains syndromes in trauma victims. However, it seems to be an underutilized adjunct treatment to accelerate fear extinction in PTSD in conjunction with exposure-base therapies. Therefore, the purpose of this study is to review

literature to assess the effectiveness of auricular acupuncture, as vagus nerve stimulation, for the possible treatment of PTSD conditioned fear.

For this narrative literature review, two comprehensive searches were conducted:

The first, to investigate the evidence of VNS for fear extinction.

The second, to assess the effectiveness of VNS with acupuncture. The primary database searched was Pubmed, followed by an additional search in EBSCO, Hindawi, ScienceDirect, ResearchGate.

For VNS and fear extinction, the keywords “VNS” OR “vagal nerve stimulation” OR “brain stimulation” OR “neuro stimulation” AND “fear” OR “fear extinction” OR “consolidation” OR “PTSD” were used as search parameters. This search yielded 91 papers published between 2010 and 2019.

For acupuncture and VNS, the terms “vagal nerve stimulation” OR “VNS” OR “Vagus Nerve” AND “acupuncture” were searched in which yielded 62 papers from 2010 to 2019. Studies more than 10 years old, non-English, non-peer reviewed, or without research studies were excluded. Studies that did not address vagal modulation, utilize VNS, tVNS, nor using auricular acupuncture points as treatment (relative to their specific search parameters) were also excluded. The final 16 articles yielded, 4 RCTs using animal subjects, and 11 RCTs using human participants and 1 systematic re-review.

The result of this narrative review provided evidence of measurable outcomes for the effectiveness of auricular acupuncture points to stimulate the vagus nerve and that this stimulation can improve fear extinction in PTSD. While there is significant evidence of auricular acupuncture modulating the autonomic nervous system more RCTs evaluating auricular acupuncture’s effectiveness in an exposure-based therapeutic setting, as well as assessing the ratio efficacy/cost of auricular acupuncture stimulation versus other neurostimulation modalities are warranted.

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INTRODUCTION

Post-traumatic stress disorder (PTSD) is a response to trauma that results in a chronic perception of threat. It is experienced by individuals after exposure to an event that elicited feelings of fear, helplessness, and/or horror. These individuals can find themselves caught in reoccurring patterns of defensive reactions to neutral situations, with an inability to shift out of this fearful state. The learned fear response in PTSD in understood to stimulate sympathetic and parasympathetic neural components of a sequential defensive cascade (Kozlawska et al., 2015), which often present as intermittent explosive disorder (fight), anxiety or avoidance (flight), and depression (immobilization) (Lamb et al., 2017)

Comorbidities are frequent in patients with PTSD because of the physiological and psychological effect of the chronic defensive posturing that can happen after trauma. The chronic stress connected with PTSD is a critical health issue, and this physiological reaction to a perceived constant threat can be clinically costly (Lamb et al., 2017).

Clinical care offers a low effectiveness rate, is often delayed, and many with PTSD go untreated (Schottenbauer et al., 2008). Posttraumatic stress disorder (PTSD) affects 7–8% of the general U.S. population at some point during their lifetime. Development of PTSD occurs in approximately 28–50% of trauma-exposed individuals. A large proportion of the PTSD seen among men in the United States is from combat exposure. However, the main burden of PTSD in the United States stems not from war or terrorism but from far more common events such as criminal victimization, motor vehicle accidents, and childhood maltreatment (physical, sexual, and emotional)(Nemeroff et al., 2006).

The total economic burden of PTSD is difficult to determine. In one study, patients diagnosed with PTSD were selected from the Veterans Health Administration (VHA) database and health care resource utilization and costs during the 12-month follow-up period were assessed and calculated. Total expenditures per individual were observed at $16,750. (Wang et al., 2016). This shows that in the military population alone, this disease is associated with high outpatient visit utilization, which translates to a high-cost burden.

There have been extensive studies on Post Traumatic Stress Disorder (PTSD) treatments. The VA/DoD PTSD Clinical Practice Guideline (CPG) for Posttraumatic Stress Disorder (2017) offers recommendations for evidence-based treatments of PTSD. The most effective of these treatments being individual trauma-focused psychotherapies stated were Cognitive Processing Therapy (CPT), Prolonged Exposure (PE), and Eye Movement Desensitization and Reprocessing (Nash & Watson, 2012). In these exposure-based therapeutic settings, a patient is trying to learn how to regulate and tolerate intense emotions. This can trigger high stages of arousal as well as possibly activate what is known as the defense cascade (arousal, freezing, flight or fight, immobility). Therefore the therapist uses cognitive, emotional, or behavioral techniques to facilitate the processing of a traumatic event to help patients shift out of this defensive state and return to a state of calm (Kozlowska, Walker, McLean, & Carrive, 2015).

These therapies, therefore, have taken on the more challenging task of transforming the "root" of the issue – the traumatic memories and the conditioning that can take initial neutral cues and then trigger strong emotional responses (Bouton, 2002). These trauma-based processes that help the mind creating new emotions and memories in place of the old traumatic one are commonly referred to as fear extinction or fear consolidation. Extinction learning does not erase initial learning, but the new learning competes with the old, eventually leading to a new situation-appropriate response, helping the patient to gradually reduce her/his fear of this cue over time. (Marian et al., 2014).

These intrusive memories and subconscious reaction to those memories have been difficult to treat because PTSD is characterized by fear that is resistant to extinction (Milad et al., 2009). This evidence suggests that the inability to extinguish conditioned fear enables the strengthening of traumatic memories over time, contributing to the development of PTSD. Two of the most studied forms of therapy, prolonged exposure therapy and cognitive processing therapy, are effective in many veterans with PTSD; however, about 30–60% of patients failed to show clinically significant improvement. (Azulay et al., 2013). Among the reasons cited for this failure include high dropout rates of 30–40% due to difficulties in tolerating the therapy, or failure to initiate therapy in the first place (Schottenbauer et al., 2008)

Numerous studies have suggested that a promising treatment strategy for fear extinction and to combat drop-out rates, is to combine trauma-based exposure therapy in a situation where the individual can remain in a calmer state and then continue to retain a parasympathetic state following the therapy. When the body senses an imminent threat like it does in PTSD, it initiates a fight-flight-response that leads to the release of peripheral epinephrine which activates beta-adrenergic receptors on the afferent vagus nerve (Burger et al., 2016). This afferent information reaches parts of the brain that will release norepinephrine (NE) in the several brain regions that support memory formation. This increased release of NE, suggests why fear memories are more strongly consolidated and therefore remembered more easily than neutral events (Cahill & Mcgaugh, 1998). Experimental studies have found that electrical stimulation of the vagus nerve leads to NE being released in the brain (Fanselow, 2013) which suggest that consolidation of extinction memory could be improved by employing the same mechanism through which a fear memory is more easily stored (Burger et al., 2018).

Low levels of vagus nerve activity have also been detected in anxiety patients [measured by vagally-mediated heart rate variability (HRV)] while higher levels of vagus nerve activity have been linked with an increase in safety learning and the inhibition of conditioned fear response (Lamb et al, 2017). Therefore as an adjunct therapy, vagus nerve stimulation holds promise because it has been shown to produce both NE memory enhancing and calming parasympathetic effects, contributing to the fear extinction in PTSD (Peña, Engineer, & McIntyre, 2013). These physiological findings continue to support the hypothesis that VNS may strengthen exposure-based therapy as well as reduce the number of exposure therapy sessions required to treat PTSD patient's defensive fear postures. (Lamb et al., 2017).

Auricular Acupuncture and the Vagus Nerve Stimulation

For thousands of years, Traditional Chinese medicine has used acupuncture points in the ear to effect change in all the organ systems of the bodies (He, et al., Auricular Acupuncture and Vagal Regulation, 2012). Acupuncture is an integral modality of traditional Chinese medicine (TCM) and has been accepted in China and used as one of the integrative and complementary treatments in western countries. Acupuncture is a technique that involves inserting and manipulating thin solid needles into specifically chosen points in subcutaneous tissue (or "acupoints") for the given period of time, which, according to Traditional Chinese Medicine (TCM), moves which is understood to move vital energy (Qi) around the restoring balance in the body and internal organ systems (Hollifield, 2011).

Acupuncture has been increasing in popularity and an important integrative approach that has been shown to be safe and effective for treating anxiety, depression, stress, chronic pain, and other symptoms that often accompany PTSD (Engel, et al., 2014). Furthermore, neuroimaging and neurophysiological studies have found that acupuncture has limbic system, prefrontal cortex, and autonomic nervous system effects (Haker, Egekvist, & Bjerring, 2000). These neurological systems have also been implicated in the development and of resistance to and consolidation of fear extinction in PTSD (Burger, et al., 2016).

More importantly, for this review, auricular acupuncture has been shown to play a role in vagal activity of autonomic functions. The auricular branch of the vagus nerve (ABVN) is one of a least four nerves innervate the anterior auricle, with the ABVN innervating 100% of the Cymba conchae and 45% Cavity of the concha (Peuker & Filler, 2002) where many acupuncture points are found. Studies also suggest that anatomical basis for the vagal regulation of auricular acupuncture stems from the afferent projections of the ABVN to the brainstem's nucleus of the solitary tract - which is essential for coordination of complex sensory information. Therefore, the autonomic and central nervous system could be modified by this proposed the "auriculovagal afferent pathway" (He et al., 2012).

OBJECTIVE

1. Main Objectives
    a. Find evidence of the effectiveness of VNS by auricular acupuncture for treating fear extinction in PTSD through a literature review of current studies.
2. Sub Objectives
    a. Show VNS is effective for fear extinction in PTSD models
    b. Provide research that auricular acupuncture points can modulate vagal related physiological process in the human body.
    c. Suggest science-based protocols for the development of further auricular acupuncture research studies and protocols specifically for addressing fear extinction in the treatment of PTSD.

LITERATURE REVIEW

Part 1: Vagus Nerve Stimulation and Fear Extinction Studies

Neurostimulation of the vagus nerve (VNS) is becoming of great interest in the treatment of disease through modulation of the autonomic nervous system, specifically the parasympathetic nervous system. In the case of fear extinction in PTSD subjects, preliminary evidence from animal and human models suggests that the VNS has a positive effect while being used during exposure therapy (Burger et al., 2018). A basic understanding of Steven Porges' Polyvagal is important for understanding the therapeutic effects of VSN. The Polyvagal Theory outlines hierarchical behavioral strategies which explain how three subsystems (circuits) of the autonomic nervous system effect general behavior. The first circuit is activated in a safe and non-threatening environment. In this subset, the (evolutionary) youngest myelinated vagus nerve is activated which engages in parasympathetic long-term survival mechanisms such as; lowering heart rate, maintaining homeostasis, supporting social communication engagement activities, and promoting growth. However, when danger is detected, the second older sympathetic-adrenal circuits are activated and engage in defense mechanisms such as fight or flight (mobilization). Finally, in a life-threatening environment is detected the phylogenetically oldest, non-myelinated vagal circuit will activate a general behavioral shutdown (immobilization) such as a drop in heart rate and the slowing bodily activity. ("Svetlana Masgutova Educational Institute | Neurosensorimotor Reflex Integration - MNRI Method," n.d.). Therefore the process of upregulating parasympathetic tone and downregulating sympathetic response through the mylenated vagus nerve could also help us understand the therapeutic effects of vagus nerve stimulation on fear extinction.

The investigation of one of the first animal studies by Pena & McIntyre was to test whether fear extinction can be improved with VNS while being exposed to the conditioned fear cues. This VNS was with a surgically and electrode cuff that was surgically attached (Peña, Engineer, & McIntyre, 2013). Transient cessation of breath was used to test the cuff's stimulation of the Vagus nerve. Sham animals underwent the same surgical procedure but the cuff was programmed to short-circuit at the level of the head implant. The male Sprague-Dawley rats were trained on an audible cue to condition fear (tones with footshock) followed extinction training for 1–10 days (tones without footshock). One group of rats was treated with VNS or sham stimulation while being exposed to the fear conditioning stimulus. The second group was also given VNS and extinction training but the in this group the VNS was performed separately from the conditioned fear cues.

Fear condition retention (FCR) was tested 24 hours after each treatment. The researchers' prominent finding was that when rats were treated by one session of VNS paired with exposure to the conditioned cues, they showed half as much freezing as sham-treated animals. They concluded that this result indicated that VNS enhanced extinction of conditioned fear, and when extinction is paired with VNS it is more rapid than extinction paired with sham stimulation. They also found that two weeks post-treatment, fear extinction was substantially improved. Indicating that the effects of VNS can continue even with a distant fear memory.

The basis of a second animal study by Pena et al. was the premise that PTSD patients show impairment in the ability for their brain to modify their fear response. This impairment of extinction of conditioned fear was linked to the decreased ventromedial prefrontal cortex (vmPFC) over amygdala activity. Neuroplasticity has been detected in the basolateral complex of the amygdala (BLA) after both the development of conditioned fear responses and the suppression of those responses during extinction. Since prior studies showed that Vagus nerve stimulation (VNS) paired with exposure to conditioned cues enhanced fear extinction in rats this new study researched whether this pairing enhances synaptic plasticity between the infralimbic (IL) medial prefrontal cortex and the basolateral complex of the amygdala (BLA) (Peña et al., 2014).

In this study, the rats' vagus nerve was also surgically equipped with a custom-made platinum-iridium wire electrode cuff. The sham group had the same surgical vagus nerve cuff, but it was designed not to deliver current. The male Sprague-Dawley rats were trained on an audible cue to condition fear task as well, followed by a retention test and 24hrs of extinction training. Vagus nerve stimulation or sham-stimulation was administered with the fear-conditioned stimulus. 24hrs later retention of fear conditioning response (FCR) was tested. After a single extinction training session, the rats given VNS exhibited a significant reduction in freezing comparable to the rats that receive 5 times more extinction sessions. Fear conditioning inclined synapses toward depression while extinction reversed this effect. In neuroscience, long-term potentiation (LTP) is a persistent strengthening of synapses based on recent patterns of activity. VNS delivered during extinction training resulted in LTP in the IL-BLA pathway. This suggests that enhancing extinction through VNS can have a lasting effect on synaptic plasticity, which is critical for extinction learning. In summary, the results indicate that "VNS promotes plasticity in the IL-BLA pathway to facilitate extinction of conditioned fear responses (CFRs)" (Peña, et al., 2014) .

A third animal study by Noble et al. was based on these findings of enhanced plasticity with VNS treatments. They examined whether vagus nerve stimulation (VNS) supplements extinction of conditioned fear and reduces PTSD-like symptoms in rats subjected to a single prolonged stress (SPS) protocol, which models PTSD trauma. The SPS was restraint, forced swim, loss of consciousness, and 1 week of social isolation. The rats subjected to SPS showed impaired extinction of conditioned fear like that found in PTSD patients. After the SPS process and 1 week of isolation, the rats underwent auditory fear conditioning (AFC) followed by extinction sessions. During half of the 11 fear extinction days (every other day), VNS or sham stimulation was administered with the conditioned stimulus. The VNS was again applied by a surgical cuff on the cervical level of the left vagus nerve to avoid the sinoatrial node on the right. One week after completion of the 11-day extinction process, rats were given various behavioral tests to evaluate anxiety, arousal, and avoidance. The results showed that after eleven consecutive days of extinction, the non-VNS rats given SPS one week prior to the AFC failed to terminate the freezing response. The rats without SPS exposure and those with SPS exposure revealed similar levels of conditioned fear following AFC. Although animals with SPS demonstrated significantly higher levels of freezing response to the conditioned stimulus, those rats did not reach remission of conditioned fear (<10% freezing to the CS) without the administration of VNS. On extinction day 5, 7, 9 and 11 to the completion of treatment, PTSD (SPS) model rats given VNS showed decreased freezing versus (SPS) rats given sham stimulation. Therefore, the study concluded that VNS treatment led to the remission of freezing behavior caused by CS in PTSD model rats.

Furthermore, the results showed VNS reversed the impaired extinction and decreased reinstatement of the conditioned fear response. The experiments also indicated VNS treatment during extinction could eliminate PTSD-like symptoms, such as anxiety, hyperarousal, and social avoidance, for one week after VNS treatment. Therefore, researchers findings suggest that VNS may be a useful adjunct treatment with exposure therapy for the treatment of PTSD (Noble et al., 2017).

The second animal study by Nobel et al. conducted two research inquiries (with 4 experiments) (Noble et al., 2019). One trial investigated whether VNS could generalize extinction for a stimulus (sound or smell) that wasn't present during the extinction process but was connected with the fear event. If so, it could show increased support for VNS in the therapeutic process of fear extinction since the ability to produce all trauma stimuli in PTSD is difficult. The second was to test VNS effects on anxiety. In the first trial, three experiments were formulated to determine whether VNS with conditioned cues promotes generalization of extinction. In experiment one, rats underwent auditory fear conditioning (AFC) where two discernable stimuli (sounds) were presented during the same conditioning session. Both sounds were paired with footshocks. Only one of the stimuli was presented during the extinction treatment day, but both were presented during testing sessions. In the second experiment, the two stimuli were conditioned in separate sessions (one sound per session) on different days. In the third experiment, the stimuli were different as well as different contexts (smell, lighting, location). Half of the animals received VNS, and half received sham stimulation during the relative extinction sessions. The researchers found that only when the two sounds were coupled with footshock in the same extinction session did VNS generalize extinction (of both sounds). There was no generalize extinction when conditioning of the two sounds occurred on different days or different contexts. A fourth experiment was also performed to test VNS effects on anxiety. Rats were treated with VNS or sham stimulation prior to being tested on an elevated maze. The rats that were treated with VNS spent significantly more time in the open maze. These results indicate anxiety can be reduced within minutes of a 30-sec treatment of VNS. The overall conclusion was of the results of the first three experiments is that VNS can promote generalization of extinction to other stimuli that are associated with a specific fear experience. Furthermore, VNS itself, without fear extinction, appears to reduce anxiety. Because of this ability generalize extinction and reduce anxiety, VNS is proposed as a credible candidate for use as an adjunct therapy to improve the "efficacy and tolerability of exposure-based therapies" (Noble et al., 2019).

Based on earlier animal experiments, Burger et al. conducted a study with human subjects, with the hypothesis that stimulation of the vagus nerve can enhance memory formation in humans as well as animals (Burger et al., 2016). The intent of this study was to assess whether transcutaneous stimulation of the vagus nerve (tVNS), rather than surgical implantation, can also facilitate fear extinction and retention in humans with fear conditioning. In a randomized control trial, thirty-one healthy participants (30 female, 8 male, average age of 21) were subjected to the controlled stimulus of sound (colored shapes), and uncontrolled stimulus (scream, white noise). After this fear conditioning, participants were randomly assigned to receive sham or tVNS stimulation during their extinction phase. The tVNS device used had two titanium electrodes to provide electrical stimulation, which were positioned on top of a silicon earplug and connected to a small neurostimulator. The decision was made to stimulate the left ear's concha – one, to avoid cardiac effects of the right ear's efferent vagal fibers and secondly, the concha because of the vagus nerve innervation (Peuker & Filler, 2002). The electrodes simulated 30-second electrical waves (0.5mA, 25Hz) alternating with 30-second breaks. The electrodes in the sham procedure were connected to the center of the earlobe because the vagus nerve does not innervate the earlobe (Peuker & Filler, 2002). Retention of extinction memory was tested on the second day. The participants were assessed for US expectancy ratings, fear-potentiated startle responses and phasic heart rate responses. Based on the results, the researchers concluded that tVNS did improve fear extinction learning (US expectancy ratings). However, their acquisition of the physiological fear responses was unsuccessful which made testing whether tVNS also facilitates the extinction of those fear responses (startle and cardiac) unavailable. Also, the US expectancy ratings only showed the effect by tVNS during the stimulation period but observed the return of fear for both conditions on the next day. However, with the limitations, these study stated these results could supplement recent studies that suggest vagus nerve stimulation could be a promising method to improve memory consolidation and fear extinction (Burger, et al., 2016).

A secondary study by Burger and colleagues (Burger et al., 2017) aimed to further investigate effects of tVNS during extinction training in healthy humans using a different model than their previous study (Burger et al., 2016). First, this new study used an electro-cutaneous stimulus as an uncontrolled stimulus (US), instead of the auditory US used previously, in order to ensure fear learning. Second, to ensure sufficient time for the acquisition and extinction consolidation, they tested acquisition, extinction, and retention of extinction on three separate days. Furthermore, in contrast to the previous study, the researchers specifically paired tVNS with the extinction learning trials strategizing that this had yielded the strongest effects in the animal studies by Pena et al. (Peña et al., 2013). The main hypotheses for this second study were that tVNS would accelerate the extinction of both declarative and psychophysiological fear responses. Additionally, they theorized that tVNS would increase the consolidation of extinction memories, in contrast to what was found in the previous study (Burger et al., 2016) but consistent with animal studies on the effects of VNS on fear extinction (Peña et al., 2013). The research tested whether stimulating the auricular branch of the vagus (transcutaneous VNS; tVNS) accelerates extinction and reduces the spontaneous recovery of fear. This 3-day fear condition study, 42 healthy students participated were randomly chosen to receive sham or tVNS stimulation on the concha of the left ear. The stimulation was paired with the controlled stimulus (CS), which was two geometrical figures presented on a computer screen with a black background. The uncontrolled stimulus was the electrocutaneous shock on the leg and acoustic startle. Day 1 of the study fear acquisition was tested, the second day fear extinction, and the third day retention of the extinction memory was tested. Also, in contrast to the previous study, all participants received sham stimulation during the acquisition and retention phases to control variance in context. Fear indexes tested included US-expectancy, skin conductance responses, and startle blink EMG. Although the psychophysiological indexes showed no clear effects of tVNS on extinction and retention of extinction, the results did show successful acquisition and extinction of fear. The tVNS facilitated the extinction of declarative fear shown by US expectancy ratings, but like the previous study, did not promote stronger retention of the declarative extinction memory. The researchers conclude that tVNS may positively affect learning and memory in a fear extinction model called for more large scale studies to assess the effects of tVNS on fear-related learning processes, including extinction and retention learning (Burger et al., 2017).

A tertiary, human, single-blinded controlled trial by Burger and colleagues intended to evaluate the effects of tVNS on both physiological and declarative fear extinction in a large enough sample size in order to detect meaningful statistical effects. Similar to their previous studies (Burger et al., 2016), the fear acquisition and extinction phases were conducted on the same day. For the control stimulus, pictures of spiders were chosen to have a more pronounced fear response and delayed fear extinction. Other differences in this experimental model, from previous, were the addition of background noise and increased startle probe intensity also to increase physiological arousal and strengthen fear conditioning. These changes were employed to slow down fear extinction, which could allow for a stronger difference between the effect of tVNS compared to sham stimulation. After a fear conditioning phase, 85 participants were randomly chosen to receive tVNS (final N = 42) or sham stimulation (final N = 43) during the extinction phase. Conditioned fear was evaluated using US expectancy ratings, skin conductance, and fear-potentiated startle responses. Participants in both groups, after successful fear acquisition, exhibited a reduction of fear throughout the extinction phase. However, there were no differences between the groups in extinction rates for physiological fear indices. Also, contrary to previous study results, participants in the tVNS procedure did not display accelerated declarative extinction learning. The researchers stated the results could indicate enhanced safety cues because the tVNS group's CS trials did have lower initial US expectancy ratings than those who received sham stimulation. However, the study concluded that because the expected accelerated extinction due to tVNS was not observed more research on tVNS optimal stimulation intensity setting is called for (Burger et al., 2018)

The authors of this next study stated concern because of the large proportion of PTSD in the military personnel, often preceded by a mild traumatic brain injury (mTBI), do not often achieve clinical response or remission through treatment (Lamb et al., 2017). They conducted a single visit pilot study on the reported impact of tVNS on many human brain regions associated with the development and expression of PTSD and the autonomic state, which is associated with fear and fear response. The premise being that posttraumatic stress disorder (PTSD) is a reaction to trauma that results in a chronic perception of threat, triggering mobilization of the autonomic nervous system, and may be echoed by chronic disinhibition of limbic structures (Williamson et al., 2013). Therefore, the current study was designed to evaluate the impact of tVNS on hyperarousal indicators incorporating vagal tone, measured by high-frequency HRV, and sympathetic nervous system activity shown by emotionally modulated startle as measured by skin conduction changes. Lamb and al., hypothesized that vagal tone would increase and that emotionally modulated sympathetic nervous system activity would lessen in response to tVNS. Also, acknowledging that a common injury preceding PTSD in veterans is mild traumatic brain injury (mTBI) and that this may be due to the vulnerability of white matter in these networks and such damage may affect treatment response. In this study evaluated the impact of tVNS in 22 combat veterans that were either diagnosed with PTSD with preceding mTBI or healthy controls. Participants completed a posturally modulated autonomic assessment and emotionally modulated startle paradigm. During the tilt-table procedure, respiratory sinus arrhythmia (RSA) as measured by high-frequency heart rate variability was recorded, and skin conductance changes were monitored and recorded during the acoustic startle in response to emotional images (International Affective Picture System). Participants were randomly selected for either tVNS or sham (stimulus calibration only) subgroups and were fitted with custom tVNS electrodes and had threshold calibration for participant comfort. In the sham group, the stimulus amplitude was set to 0 while in the tVNS, the stimulus amplitude was set to 80% of pain threshold. Both groups participated in the series of assessments of ANS function: emotionally modulated startle and postural HRV assessments. The results showed that the mean RSA was higher in the tVNS group than the sham group, across all three tilt-table postural positions which indicate the increase in parasympathetic activity. Furthermore, the electrodermal responses (EDA) during the startle response in the tVNS group showed a trend of reduced reactivity of the sympathetic nervous system in response to emotionally modulated startle. The studies preliminary findings, as stated by Lamb and colleagues, are that tVNS can increase resting parasympathetic activity and decrease emotionally modulated sympathetic nervous system activity. Also stating that these results show tVNS direct impact on the PTSD hyperarousal symptom, not only to downregulate fight-or-flight but also to upregulate a physiological state that is conducive to positive social engagements. Therefore, since the tVNS was well tolerated and affected systems underlying emotional and neurological dysregulation of the PTSD population, it should be further evaluated and developed as a potential treatment tool for these patients. (Lamb et al., 2017).

Part 2: Vagus Nerve Stimulation through Auricular Acupuncture

In traditional teaching of Chinese Medicine, the external auricle of the ear corresponds to parts of the body and organ system. The theory also imparts that a dysfunction of the organs can causes changes in the corresponding area in the external ear such as a painful spot, decreased tissue density or resistance with palpation, and reduced electrical resistance. And alternately by stimulating those areas would treat the underlying organ pathology or pain in that area (Gao et al., 2012). However, the mechanism behind the effect of auricular has still not been entirely ascertained or universally accepted (Asher et al., 2010).

In 1832, Friedrich Arnold, a German anatomy professor, found that stimulation the external ear canal could cause a cough that was similar to the cough reflex induced by the vagal nerve. They called this reflex the “Arnold's Reflex” and therefore considered the Auricular Branch of the Vagus Nerve (ABVN) as a Vagal afferent nerve (He et al., 2012).

The re-analysis by Usichenko, Hacker & Lowe of the data in “Auriculotherapy for Pain Management: A Systematic Review and Meta-Analysis of Randomized Controlled Trials” (Asher et al., 2010) has importance for this research because it further supports the hypothesis of auricular acupuncture as a means to stimulate the vagus nerve. The original paper being review was a meta-analysis of 17 RCTs on the effectiveness of AA in the treatment of patients with acute and chronic pain. Usichenko, Hacker & Lotze conducted a new review to understand and clarify the mechanism of auricular acupuncture in treating acute and chronic pain with regard to current knowledge of the external auricles neuroanatomy. (Usichenko, Hacker, & Lotze, 2017). The researchers plotted the specific AA and sham points from the 17 RCTs over an anatomical drawing of the outer ear. The plotting of the innervation of the external ear was taken from an investigation of Peuker and Filler, 2002. The data of the auricular innervation was ascertained through cadaver anatomic dissection under magnifying glasses after the dyeing of the nerves (Peuker & Filler, 2002). The result was that fifteen out of 20 AA points used for pain in the 17 RCTs, were either situated in the areas innervated exclusively by cranial nerves or had mixed innervation of the auricular branch of the vagal nerve (ABVN) and cervical nerves (Appendix B). Shenmen (1), Lung (2), and Thalamus (3) were the most frequently used to treat pain and were also located in the area of mixed innervation by the ABVN and the cervical nerves (Appendix A). The sham stimulation was mostly applied in the area innervated by the cervical nerve, mainly at the helix and lobulus of the auricle. The researchers concluded that considering that the empirically specified AA points received cranial nerve afferent innervation that the analgesic effects of AA can be explained by stimulation of ABVN (Usichenko, Hacker, & Lotze, 2017).

Vagal stimulation of the Cardiovascular System

The vagus nerve has cardiovascular effects and will typically cause a reduction in heart rate and blood pressure (McCorry, 2007). A sophisticated and noninvasive way to assess the parasympathetic nerve activity of auricular acupuncture is to test heart rate variability (HRV). Low frequency (LF) fluctuations that are in the range of 0.04–0.15 Hz would be considered markers of sympathetic nerve activity, while high frequency (HF) fluctuations that are in the range of 0.15–0.4 Hz would be considered parasympathetic nerve activity markers. The aim of the study by Arai, et al. was to see the effect on postoperative heart rate variability (HRV) from auricular acupuncture applied to "Shenmen" and "Point Zero" points (Appendix). Twenty-six hemicolectomy patients were randomized into an acupuncture group or a control group. The control group received no treatment while occlusive press needles were applied to the acupuncture group after the operation and before coming out of anesthesia. An electrocardiographic unit was used to record the autonomic nervous activities. The results were low frequency (LF)/high frequency (HF) ratio of HRV increased ($P = 0.0007$) in the control group, but the ratio in the acupuncture group did not change. The HFs of the acupuncture group were found to be significantly higher than those of the control group. The hypothesis of the researchers was that they could see a change in autonomic nervous activity during the postoperative period as these particular auricular acupuncture points would "tranquilize the mind" of patients. They concluded that throughout the post-operative period, acupuncture kept the LF/HF ratio at lower levels and HF at higher levels thereby showing effects of auricular acupuncture on the autonomic nervous activity (Arai et al., 2013).

Another investigation on auricular acupuncture and cardiac function focused on the relationship between auricular acupoint "Heart" (14 - Appendix B) and cardiovascular regulation. This pilot study by Gao et al. was testing a vibrational stimulation system for ear acupressure and its effect on heart rate (HR), heart rate variability (HRV) as well as pulse wave velocity (PWV), and the augmentation index (AIx). With new software, the researchers were able to analyze and display the HRV in a new way that they could evaluate the function of the autonomic nervous system. This study also was collecting the mean HR, the total HRV, and the LF (low frequency)/HF (high frequency) ratio of the HRV to demonstrates how well the human body reacts to acupuncture. Pulse wave velocity (PWV) is recognized as a marker of arterial stiffness while the augmentation index (AIx) is more often used as a parameter of wave reflection. 14 healthy subjects were selected which included 9 females and 5 males. The stimulation was done at the “heart” auricular point with a pen that was specifically equipped with an electronic device to provide vibration at a frequency of about 30 Hz. The tests were conducted before during and after the manual acupressure (pen without vibration) and vibrational stimulation. The results of this study showed that the HR decreases ($P \leq 0.001$) and HRV total increased significantly ($P = 0.008$) during ear acupressure vibration and/or manual ear acupressure. The pulse wave velocity between the bifurcation of the aorta and the aortic root was decreased and, after vibrational and manual acupressure at the “heart” auricular acupoint, the augmentation index immediately increases. The researchers’ hypothesis is that ear acupressure can influence the autonomic nervous system and these ear stimulation methods could possible cause “measurable, reproducible physiological alterations, especially of HR, HRV, and blood pressure, as well as changes in the parameters of human arterial stiffness and wave reflection”(Gao et al., 2012).

In addition to these studies, another study had some conclusive results regarding the sympathetic nervous system and auricular acupuncture. The Kung, Yang, Chiu, & Kuo study was to examine how the change in cardiac sympathovagal activity by auricular acupuncture (AA) therapy would be related to the change in self-reported insomnia in postmenopausal women. Taipei Veterans General Hospital, Taiwan conducted a pretest/posttest study design of forty-five women. These women were the average age of 56 and had been suffering from postmenopausal insomnia for 3 to 5 years. For four weeks these women received an auricular acupressure course on five auricular points every night before going to sleep. Heart rate variability (HRV), the Menopause Rating Scale, and the Chinese version of the Pittsburgh Sleep Quality Index were measured before and after each AA treatment.

All participants received a subjective sleep quality questionnaire and HRV measurements before the AA treatment. A baseline HRV measurement was taken for 5 minutes, from 9 to 11 am while the participant was resting quietly. After the HRV measurement, 5 magnetic pellets with sticky backs were applied by a licensed acupuncturist on five auricular points: Shenmen, kidney, heart, brainstem, and subcortex (Appendix B). The participants instructed to press on each point every second for 1 minute (60 times) every night before going to sleep. The same subjective sleep quality questionnaire and HRV measurements were recorded after a 4-week of auricular acupressure therapy.

After the 4-week therapy, there was a moderate correlation between a greater percentage change in Pittsburgh sleep quality index with both a higher percentage change in normalized low frequency (LF) power of HRV as well as a lower percentage change in high frequency (HF) power of heart rate variability (HRV). These results suggest that auricular acupuncture therapy led to more parasympathetic and less sympathetic cardiac activities. Thus contributing to the improvement in these women of their postmenopausal insomnia. (Kung, Yang, Chiu, & Kuo, 2011).

Wang et al. conducted another similar study on auricular acupuncture on insomnia. This study also examined auricular acupressure's effect on heart rate (HR) and heart rate variability (HRV) in patients with chronic insomnia. 31 patients (6 male, 25 female) with chronic insomnia were selected. Again, the auricular acupoint "Shenmen" was selected for acupressure stimulation. A seed (Semen vaccariae-Wang Bu Liu Xing) with adhesive plaster was applied at "Shenmen" on the left ear. The auricular acupressure was performed for 30 pressure movements per 15 seconds. This procedure was done every 10 minutes, for a total of 3 times. The researchers concluded that the HR significantly decreased during and after the acupressure treatment. However, they noted that the effect only appeared in the second phase of the acupressure (10 minutes after the first stimulation). The total HRV also showed a significant increase with stimulation but with no long-lasting effect (Wang et al., 2013).

A different acupuncture study investigated that studied AA ability to influence the autonomic nervous system through monitoring of HRV. This study by Shi et al. into what the acceptability and the impact would be of providing continuous auricular electroacupuncture as an integrative therapy along with conventional medications for patients with depression. This study monitored HRV while having acupuncture treatment. This small study included ten patients with a median age of 43 Ten patients suffering from depression with a mean age of 43.3 (range of 29–59 years). All patients started the experiment in the morning with the clinical evaluation performed directly after the first HRV recording. The evaluation used three main scales: the Hamilton rating scale for depression (HRSD, the Athens insomnia scale (AIS), and the Hamilton anxiety rating scale (HAM-A),. None of the patients were on medication or had a history of any cardiovascular issues. Their heart rate (HR), heart rate variability (HRV), and different clinical scores were the quantitative and qualitative outcome measures. This study was the first to use a miniaturized system "P-stim" application pointer to supply a continuous electrical stimulation at an ear acupoint in patients suffering from depression. Ultrathin permanent needles were applied at the ear with a generator located behind the ear that produces electrical stimulation impulses. The unit was applied by a Chinese physician using acupuncture points Shenmen, Small Intestine, and Heart. After 24 hours of this continuous electrical stimulation, the study found that all clinical scores (HAM-A, AIS, HRSD) showed a significant improvement. HRV was also found to improve significantly. The study documented that 3 days of auricular electro-acupuncture can improve various aspects of quality of life significantly. (Shi et al., 2013).

Vagal Stimulation Of The Respiratory System

A 2010 study (Marca et al., 2010) used a three-armed randomized trial to evaluate the effects of electro-acupuncture on vagal activity by monitoring respiratory sinus arrhythmia adjusted for tidal volume (RSA_{TR}). In this trial, fourteen healthy men from 20-40 years of age were recruited from two Zurich universities with exclusion criteria of depression, acute and chronic psychiatric disorders, medication within the last two months or consumption of psychoactive substances of or excessive alcohol consumption. They were instructed not to drink caffeine for 48 hours, as well as avoiding any excessive physical exercise and/or smoking for 24 hours. They were also instructed to avoid eating 2 hours prior to their treatments. They participated in four examinations in random order (without repeat): a condition with placebo, a control condition without intervention, as well as manual and electroacupuncture. Because of the neuroanatomical evidence of afferent vagal innervation, acupuncture was used in the left ear's cavum conchae inferior. Placebo and verum needles were inserted into this concha area, which also corresponds with the lung and heart points. In all acupuncture sessions, two needles were placed 5 mm apart to allow for an electrical flow and to keep an equal number of needles in all interventions. The experiment was considered partially blind. The participants were blinded regarding the kinds of acupuncture therapies, the application of placebo needles, and about the expected effects of acupuncture. The examiner was blinded until the end of the habituation and baseline period but was no longer blinded when they applied the needles with or without electrical stimulation. At that time they were instructed to behave identically as the other conditions. The examinations took place once a week with each examination lasting 90 min, which consisted of 30 min of habituation and baseline measurement, then 30 min of one of the 4 intervention and 25 min of postintervention. Respiratory sinus arrhythmia adjusted for tidal volume (RSA_{TR}) was measured continuously for indicating vagal activity. Baseline levels of cardiovagal activity were tested to control for successful randomization and revealed no significant differences between the different conditions (RSA: 0.280 <P<0.889; RSATR: 0.277 <P<0.898). The researchers' final conclusion, controlling many adverse effects, was that auricular electroacupuncture but not manual auricular acupuncture showed a positive effect on RSA_{TR} (Marca et al., 2010).

Auricular Acupuncture, CBT and PTSD

A new randomized control study (RCT) by Feng and al. was published in April 2019. The study includes 240 patients that were treated for PTSD symptoms by transcutaneous electrical acupoint stimulation (TEAS). The researchers' objective was to determine whether adding TEAS to sertraline or cognitive behavioral therapy (CBT) could improve anti-PTSD efficacy (Feng et al., 2019). 60 people were randomly assigned a group: Group A received stimulated TEAS that was combined with steraline. Group B received stimulated TEAS with CBT. Group C received active TEAS combined with CBT, and Group D received active CBT with sertraline. The treatment was administered over the course of 12 weeks. The Clinician-Administered PTSD Scale, PTSD Check List-Civilian Version, and 17-item Hamilton Rating Scale for Depression were used to measure outcomes.

The study found that while PTSD symptoms were reduced over time in all patients groups that the active TEAS groups showed greater improvement. Those groups (groups C and

D) specifically showed greater improvement in both depression and PTSD measures than group A and B. This improvement was in all post-baseline measurement points, with what was stated as a moderate to very large effect sizes of 0.484-2.244. C and D groups clinical response and remission also had a significantly higher rate than groups A and B. The clinical results rate was (85.0% and 95.0% vs 63.3% and 60.0%, $P < 0.001$) respectively, with the remission rate comparison of (15.0% and 25.0% vs 3.3% and 1.7%, $P < 0.001$). Adverse events reported were similar between groups A and D and between groups B and C. The study concluded that "TEAS augments the anti-PTSD and antidepressant efficacy of antidepressants or CBT, without increasing the incidence of adverse effects" (Feng et al., 2019). This trial was registered with www.chictr.org (no.: ChiCTR1800017255).

MATERIALS AND METHODS

Literature search

For this narrative literature review examining the effectiveness of auricular acupuncture to stimulate the vagus nerve to treat fear extinction in PTSD. Searches were conducted to investigate first the evidence of VNS and fear extinction followed by VNS and acupuncture. The primary database searched was Pubmed, followed by an additional search in EBSCO, Hindawi, ScienceDirect, ResearchGate.

For acupuncture and VNS, the terms "vagal nerve stimulation" OR "VNS" OR "Vagus Nerve" AND "acupuncture" were searched in which yielded 62 papers from 2010 to 2019.

For VNS and fear extinction, the keywords "VNS" OR "vagal nerve stimulation" OR "brain stimulation" OR "neuro stimulation" AND "fear" OR "fear extinction" OR "consolidation" OR "PTSD" were used as search parameters. This search yielded 91 papers published between 2010 and 2019.

The references of included full-texts were also screened to include relevant papers that met inclusion criteria but had not been captured by the initial search string. This led to the inclusion of 16 research papers.

Inclusion Criteria

All titles and abstracts were screened for relevancy before reading full papers.

All original research articles, RCTs, blind or partially blind trials, and systematic reviews were included in the search that referenced the vagal nerve and acupuncture, regardless of disease or diagnosis in the first screening. There was no discernment made between auricular manual acupuncture, electroacupuncture, or acupressure. In summary, the inclusion criteria were studies performed between January 2000 and December 2019, studies reported in full text English articles that were peer-reviewed and studies involving subjects that were treated with auricular acupuncture or acupressure with vagal nerve related outcomes. (see fig. 1)

For VNS and fear extinction all original research articles, RCTs, blind or partially blind trials, and systematic reviews were included that referenced a combination of the search words. Animal studies were included because of the relatively new research paradigm. In summary, the inclusion criteria were studies performed between January 2010 and December 2019, studies reported in full-text English articles that were peer-reviewed and studies involving subjects that were treated VNS or tVNS with fear extinction related outcomes. (see fig. 2)

Exclusion Criteria

In the Acupuncture and VNS search, excluded included any literature that did not reference both search keywords, was not available in a full text after multiple attempts, was not translated into the English language, was not relevant to the autonomic nervous system, was not auricular acupuncture points, or did not reference research studies. Animal studies were not used for this section of research. One exception to the auricular acupuncture exclusion was made for a recent study from China because of the combination of cognitive behavior therapy and electro-acupuncture and because the full text was available in English. (see fig. 1)

For the VNS and Fear Extinction search: Exclusions were any papers that did not reference fear extinction, anxiety disorders or PTSD, were not Vagus nerve stimulation, were not available in a full text after multiple attempts, studies of other types of cranial nerve function, were website articles exclusively, or did not reference research studies.

Some studies referenced in this paper, particularly systematic reviews that were performed outside the United States in the last 10 years but did not have full texts available in English are still referenced in the introduction and discussion but are not considered part of the "inclusions" for the purpose of this research project.

Study Evaluation

The study design is a narrative review. Based on the exclusion and inclusion criteria, full texts of eligible studies were obtained from one of the five previous databases and reviewed. They were separated between acupuncture studies and tVNS studies and then categorized based on their study types: RCTs, systematic reviews/meta-analyses, pilot studies, and qualitative studies. The data from the studies were extracted and compared. The following items were extracted: Authors, Study Purpose, Patient Population, Experimental Treatment, Results/Conclusions.

Search A: VNS AND Acupuncture

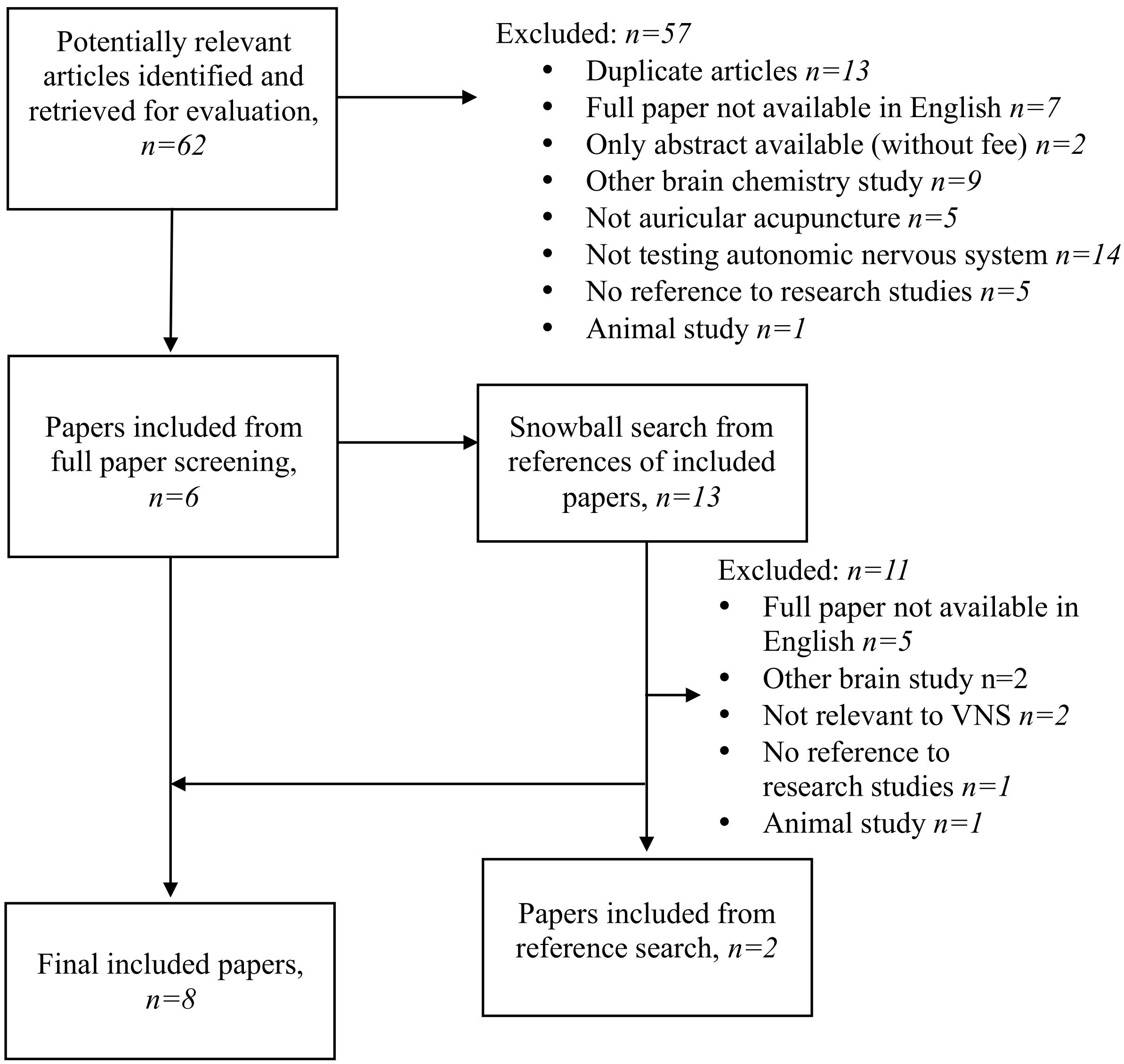

FIGURE 1 Article Inclusion Flow Chart

Search B: VNS AND Fear (Extinction)

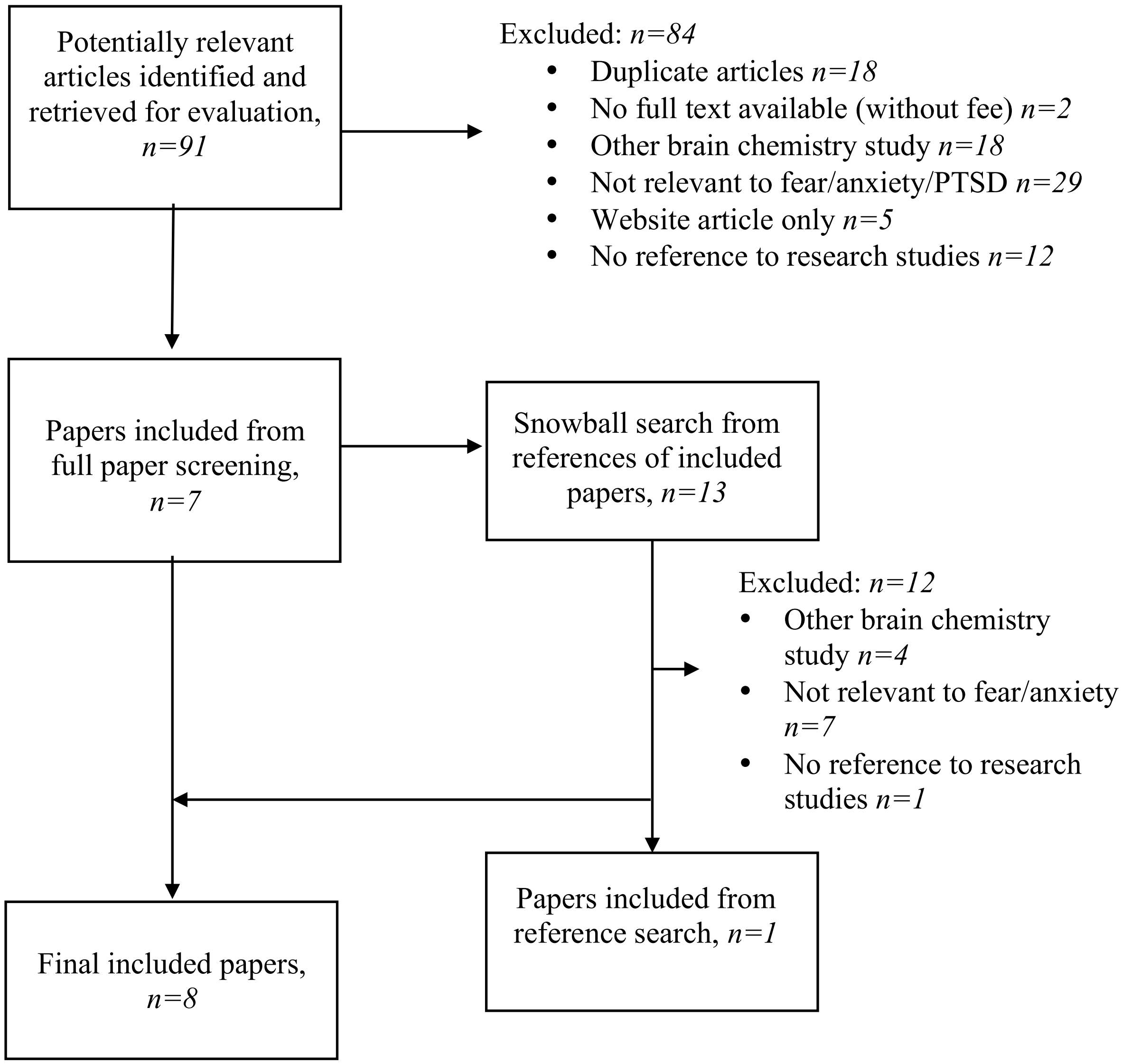

FIGURE 2 Article Inclusion Flow Chart

RESULTS AND DISCUSSION

PTSD is a complicated pathology with many associated comorbidities. Like all psychological and physiological based pathologies, the answer to therapy is not clear and simple. Acupuncture has been promoted as a way to affect not only the body, but the "shen" (emotional mind), and spirit. Though the mechanisms of acupuncture are still researched and debated, the treatment modality has a long history of therapeutic consistency. It is therefore logical to this researcher that acupuncture as an adjunct modality to any physio-psychological disturbance could be effective. The results of this narrative review are to show evidence to support this theory.

To clarify the results of these many studies, it is necessary to describe that terms used for the evolutionary adaptive response to fear, real or imagined, explained by the long-accepted Pavlovian conditioning theory. Whereby, a neutral conditioned stimulus (CS) when paired with a characteristically aversive stimulus (US or unconditioned stimulus) will cause the CS to produce a learned or conditioned fear response (CFR). This adaptive form of Pavlovian "fear conditioning" allows the individual to learn from their aversive experience but also can lead to PTSD – that is, prolonged fear responses in the absence of clear threat (Lamb et al., 2017).

This inherent nature of holding on to fearful memories creates obvious difficulties in treating the memories and the resulting defensive behaviors. However, increased insight into the neurological basis of fear has generated much interest in neuromodulatory techniques for targeting areas of the brain involved in fear extinction and learning. As shown in part by the results of the literature search explained above. The stimulation of the vagus nerve has become particularly thought-provoking as an adjunct therapy because of the preliminary results from animal and human fear condition studies.

The first two animal studies, by Peña and colleagues, on the effects of VNS on fear extinction displayed positive results. Both showed that the VNS treated rats exhibited a significant decrease in conditioned fear response (freezing) and the retention of CFR after two weeks. It is important to note that these results only presented in the rats that were treated with VNS while being exposed to the CS during their extinction training. The rats that did not have that pairing, or received the sham surgery, did not display the same improvement. This supports VNS in a context where stimulation is paired with a CS in exposure-based therapy. The second 2014 experiment was also significant because not only replicated the fear extinction results but it also presented evidence of increased brain plasticity in the area associated with fear memory consolidation (basolateral amygdala pathways). This discovery would support to retain fear extinction when VNS is combined with exposure-based therapies.

These studies were followed up by two more animal experiments by Noble and colleagues. The results of these studies provide more evidence that VNS paired with CS exposure could enhance the extinction of conditioned fear and the retention of that extinction. Additionally, it indicated that it could also increase extinction for a non-treated CS that was associated with the fear event — thereby showing a "generalized" effect of a CS treated by VNS, This would be helpful in a real-world setting where multiple stimuli could instigate a defensive fear response yet could be difficult to replicate all fear-arousal stimuli in a therapeutic session. However, the rats treated with VNS alone did not show the extinction of conditioned fear without the pairing of a CS which suggest this "generalized" effect is not of all fear but fear related to a certain condition. However, the rats treated with VNS before the open maze test did show a reduction in anxiety – which could lead pre-treating contributing to better toleration of the stress during exposure-based therapy.

Although these studies are promising and have lead to further human studies, there are obvious limitations. First, these experiments utilized a surgically implanted cuff, which is invasive and expensive for a routine treatment – an issue dealt with in resulting studies. Secondly and more importantly, the animal component – as effective as a treatment can be in rats, humans will always offer a more complicated physiological and psychological paradigm in the treatment of fear and anxiety, including a subjective component, as the continued discussion of results will show below.

Animal studies paved the way for human VNS studies as vagal innervation of the outer ear, specifically the concha, was shown to be a safe method to stimulate the auricular branch of the vagus nerve through transcutaneous VNS (tVNS) (Burger, et al., 2016). However, the result of three separate randomized single-blinded controlled trials of tVNS on humans for fear extinction and retention were mixed (Burger, et al., 2018). In the first 2-day study, the participants (n=31) that were treated by tVNS showed increased declarative fear extinction learning than those that received sham stimulation. However, twenty-four hours after fear extinction, no effect on retention of fear memories was determined. Also, tVNS effects on physical indications of fear could not be evaluated due to technical issues during the fear conditioning phase (Burger, et al., 2016). The second study (n = 39) was a three-day protocol where acquisition, extinction and retention of extinction occurred separately on consecutive days. Again, participants who were treated with tVNS showed improvement in declarative fear extinction but no retention of that improvement twenty-four hours later. Again, the effects of tVNS on physical indicators of fear extinction were not found. For the third study, Burger and colleagues surmised that a larger population of participants (n=85) could provide more statistical analysis to detect meaningful differences. Similar to the first study, fear acquisition and extinction phases were conducted on the same day. They chose pictures of spiders as the CS, to lead to more marked fear responses and therefore delayed fear extinction. With the same reasoning, they also added background noise and increased startle probe intensity. The results not only showed no effect of tVNS on the rate of declarative fear extinction, nor did it show any of the physiological indices of fear (Burger et al., 2018). The researcher considered one possible explanation for the lack of effects of tVNS on fear extinction learning was that the vagus nerve had been activated through adrenergic pathways in both conditions, rather than the predicted modulation of vagal noradrenergic activity, as a result of the increased arousal experienced by participants in the more aggressive conditioning paradigm.

Furthermore, the negative fear extinction findings could be a reflection of using spider pictures. A study using aversive stimuli (pictures mutilation and injury in humans) showed evidence that just by viewing the image, there was a connection to the parts of the brain linked to the sympathetic freezing response (Kozlowska et al., 2015). The researchers did use a phobia questionnaire regarding spiders before the experiment. However, one could deduct that spider images are not neutral like a geometric shape and could, therefore, promote a physiological response on their own merit

With these variables in mind, the results show a need for more fundamental studies on the interactions of levels of arousal with the vagal processes of tVNS in humans, since this could strongly affect the clinical applicability of tVNS (Burger et al., 2018). Furthermore, since the duration of the studies and the number of participants were limited, further study into the frequency, duration, and intensity of the stimulation will be needed to establish the whether or not it tVNS is a significantly helpful therapy for fear extinction in PTSD settings.

Table 1

VNS and Fear Extinction Studies in Rats Overview

Study	Study Purpose	Patient Population	Experimental Treatment	Results/ Conclusions
Pena et al., 2013	Enhanced conditioned fear extinction by VNS with conditioned cues	Male Sprague-Dawley Rats	Surgical electrical cuff with auditory fear conditioning and foot shock. 24 hr treatment	Lower levels of freezing behavior – improving over 10 days. VNS pairing enhances fear extinction
Pena et al., 2014	Brain plasticity enhanced by VNS for memory consolidation	Male Sprague-Dawley Rats	Surgical electrical cuff with auditory fear conditioning and foot shock and retention test. 24 hr treatment	Increased fear extinction (reduction in freezing) with evidence of increased plasticity in IL-BLA pathway
Noble et al. 2017	VNS to enhance conditioned fear extinction and improved PTSD-like symptoms	Male Sprague-Dawley Rats	Surgical electrical cuff with single prolonged stress protocol (restraint, forced swim, loss of consciousness). 5 day treatment	Reversed extinction impairment and elimination of PTSD-like symptoms for more than one week after VNS treatment
Noble et al. 2019	Generalized fear extinction with VNS	Male Sprague-Dawley Rats	Surgical electrical cuff with two separate auditory fear conditioning and foot shock. 1 day treatment	Similar freezing rate but reduction of anxiety and promotion of generalized extinction (to secondary auditory cue)

Table 2

VNS and Fear Extinction Studies in Humans Overview

Study	Study Purpose	Patient Population	Experimental Treatment	Results/ Conclusions
Burger et al., 2016	RCT: Auricular tVNS to accelerate conditioned fear extinction memory formation and retention	31 healthy participants	Visual and auditory startle and electrocutaneous stimulus. Testing US expectancy ratings, fear potential startle response, phasic heart response. 24hr tVNS treatment	tVNS accelerated explicit fear extinction but did not lead to better retention of extinction 24hr later.
Burger et al., 2017	RCT: Auricular tVNS to accelerate fear extinction and spontaneous recovery of fear	42 healthy students	Visual (geometric) and auditory startle and electrocutaneous stimulus. Testing US expectancy ratings, fear potential startle response, phasic heart response. 24hr tVNS treatment	Successful acquisition and extinction of fear and declarative fear. No retention of the declarative extinction memory.
Burger et al., 2018	RCT: Auricular tVNS to may accelerate fear extinction in healthy humans	85 healthy participants	Spider images, auditory startle and electrocutaneous stimulus. Testing US expectancy ratings, fear potential startle response, phasic heart response. 24hr tVNS treatment	No difference between groups in extinction rates for physiological indices.
Lamb, et al., 2017	tVNS for treatment of PTSD hyperarousal. Single visit pilot study	22 combat veterans – either PTSD with mTBI or healthy controls	Emotionally modulated startle paradigm. Tilt-table procedure, acoustic startle	Improvements in vagal tone and startle response

Auricular Acupuncture and VNS

Auricular Acupuncture and Acupressure (AA) interacts with the vagus nerve through the ABVN and therefore interacts with various human organs through the autonomic nervous system as evidenced in systematic re-review by Usichenko, Hacker & Lotze in 2017.

Table 3:
"Features of auricular acupuncture (AA) points in 17 randomized controlled trials included into systematic review on analgesic effects of AA" (Usichenko, Hacker, & Lotze, 2017)

Nr.	AA points	Number of RCTs, where the AA point was used	Source of afferent innervation
1	Shenmen	12	ABVN, GAN
2	Lung	7	ABVN, GAN
3	Thalamus	5	ABVN, GAN
4	Cushion	4	GAN
5	Hip	3	ABVN, GAN
6	Knee	3	ABVN, GAN
7	Lumbar Spine	1	ABVN, GAN
8	Toe	1	ABVN, GAN
9	Ankle	1	ABVN, GAN
10	Finger	1	GAN
11	Uterus	1	ABVN
12	Wrist	1	GAN
13	Elbow	1	GAN
14	Heart	1	ABVN, GAN
15	Tooth	1	ABVN, GAN
16	Mouth	1	ABVN, GAN
17	Valium	1	ATN, ABVN
18	Cingulate Gyrus	1	ATN, ABVN
19	Point Zero	1	ABVN, GAN
20	Cervical spine	1	GAN

Note: "*AA: auricular acupuncture; RCT: randomized controlled trial; ATN: auriculotemporal nerve (from trigeminal nerve); ABVN: auricular branch of vagal nerve; GAN: great auricular nerve (from cervical plexus).*" (Usichenko, Hacker, & Lotze, 2017)

The re-analysis by Usichenko, Hacker & Lowe of the data in “Auriculotherapy for Pain Management: A Systematic Review and Meta-Analysis of Randomized Controlled Trials” (Asher et al., 2010) has importance for this research because it further supports the hypothesis of auricular acupuncture as a means to stimulate the vagus nerve. Asher et al. original meta-data analysis suggested that is possible that regional specificity, and not point specificity, is responsible for some of the positive effects for auricular acupuncture points verse sham point and sn that regional innervations of the ear remain an unexplored area of investigation for auriculotherapy. Therefore the re-analysis of that data was used to specifically plot auricular acupuncture points as well as the sham points over an anatomical drawing of the outer ear. Their diagram showed that fifteen out of 20 AA points used for pain in the 17 RCTs, were either situated in the areas innervated exclusively by cranial nerves or had mixed innervation of the auricular branch of the vagal nerve (ABVN) and cervical nerves (Table 4). Shenmen (1), Lung (2), and Thalamus (3) were the most frequently used to treat pain and were also located in the area of mixed innervation by the ABVN and the cervical nerves (Appendix B). The sham stimulation was mostly applied in the area innervated by the cervical nerve, mainly at the helix and lobulus of the auricle. The researchers concluded that considering that the empirically specified AA points received cranial nerve afferent innervation that the analgesic effects of AA may be explained by stimulation of ABVN (Usichenko, Hacker, & Lotze, 2017). The limitation of this review is that it is explicitly anatomical and doesn’t present any information on needling details, treatment regimens, interventions, or controls. However, it provides a much greater understanding of the physiology of the ABVN and supports the “auriculovagal afferent pathway” of which acupuncture points in the ear can stimulate the autonomic and central nervous system through the ABVN for therapeutic purposes.

Table 4: VNS through Auricular Acupuncture Overview

Study	Study Purpose	Patient Population	Experimental Treatment	Results/ Conclusions
Arai et al., 2013	Effect of "shenmen" and "point zero" on postoperative heart rate variability (HRV)	26 patients underwent hemi-colectomy under general anesthesia	Shenmen and Point Zero with occlusive press needles post-op	LF/HF ratio lower; HF higher ratio of HRV = Acupuncture affected the HRV ratios thereby affecting ANS activity
X.Y. Gao, et al., 2012	Effects of vibration and manual acupressure on heart rate, heart rate variability, pulse wave velocity,	14 healthy volunteers	Acupressure vibration and manual acupressure at "heart" auricular acupuncture point	HR decreases and HRV total increases – more cardiac parasympathetic activities
Kung, Yang, Chiu & Kuo, 2011	Relationship in sleep symptoms/cardiac sympathovagal activity among postmenopausal women – pretest/posttest study	45 women mean age 56.2 with average 3.5 years of insomnia	AA therapy (shenmen, kidney, heart, brainstem, subcortex) every night before going to sleep for 4 weeks	HRV recordings indicated more cardiac para-sympathetic activity = improvement in postmenopausal insomnia
Wang et al., 2013	Acupressure effect on HR and HRV in patients with chronic insomnia	31 patients (6 male, 25 female) with chronic insomnia	Ear seed on Shenmen on left ear	The total HRV also showed a significant increase with stimulation but with no long-lasting effect
Shi et al., 2103	Acceptiblity and impact of continuous elecroacupuncture as therapy for depression	10 patients with depression	Continuous e-stim by "P-Stim" pointer on ultrathin permanent needles at Shenmen, Small Intestine and Heart	All clinical scores (HAM-A, AIS, HRSD) showed a significant improvement. HRV was found to also improve significantly.
Marca, et al., 2011	Effects of acupuncture on vagal activity in a three-armed randomized trial. Partially blind study	14 healthy men	electro and manual acupuncture in left ear cavum concha – 2 needle 5mm apart	Electroacupuncture and not manual acupuncture was found to have a positive effect on RSA_{TR}.

Feng and al.,	RCT whether TEAS with sertraline or CBT could improve PTSD symptoms	240 patients	Manual and electrical stim of Nei-Guan (PC6) with CBT or sertraline	TEAS augments the anti-PTSD efficacy of CBT and anti-depressants

Acupuncture point VNS and the Cardiovascular and Respiratory systems

The research presented in this narrative review has shown that auricular acupuncture, auricular acupressure and auricular acupoint stimulation has been shown to lower the heart rate and blood pressure while improving blood flow and heart rate variability (HRV). The research also showed that AA combined with electrical stimulation had a positive effect on respiratory sinus arrhythmia (RSA) by modulating vagal activity (Marca, et al., 2010). As stated previously, RSA can reflect the functional output of specific vagal pathways that are neurophysiologically and neuroanatomically linked to process such as emotion, social engagement, ingestion, and health (Porges, 2007) . Furthermore, researchers in a study by Lamb and colleagues stated that PTSD patients have reduced HRV (heart rate variability) in response to the hypervigilance caused by conditioned trauma stimuli, as well as have higher blood pressure, and require a longer recovery time than their non-PTSD peers. Unfortunately, this lowered resting HRV (RSA) is also linked to coronary artery disease and decreased nighttime RSA has been linked to increased risk of stroke risk. Lower RSA has been associated with many psychological and psychiatric disorders including generalized anxiety disorder, major depressive disorder, high levels of aggression, and trauma history (Lamb et al., 2017). Conversely, increased high frequency (0.15–0.4 Hz) HRV (RSA) is associated with improved social function, better health outcomes, and better cognitive function. Fortunately, patients who recover from PTSD have a HRV that is the same as healthy controls which suggest that the negative health effects from PTSD can be reversed if treated before the chronic stress can cause cumulative damage.

The aim of the study by Arai, et al. was to see the effect on postoperative heart rate variability (HRV) from auricular acupuncture applied to “Shenmen” and “Point Zero” points. With 26 participants, the results were low frequency (LF)/high frequency (HF) ratio of HRV increased in the control group, but the ratio in the acupuncture group did not change. However, the HFs of the acupuncture group were found to be significantly higher than those of the control group. They concluded that throughout the post-operative period, acupuncture kept the LF/HF ratio at lower levels and HF at higher levels thereby showing effects of auricular acupuncture on the autonomic nervous activity (Arai et al., 2013). The small number of participants is a severe limitation on this study as well as the ability to contain every condition throughout the post-operation process. The press needles were retained but no mention of manual stimulation during the retention period was mentioned, nor the full amount of time they were retained. Therefore it is difficult to sufficiently evaluate the positive or negative results from this study. However, it is significant that even with all these conditions that there were some positive results in LF/HF changes, which can support the vagal modulation of acupuncture, but more robust and specific trials must be completed.

Another investigation by Gao et al. on auricular acupuncture and cardiac function focused on the relationship between auricular acupoint “Heart” and cardiovascular regulation. This pilot study was testing a vibrational stimulation system for ear acupuncture and its effect on heart rate (HR), heart rate variability (HRV) as well as pulse wave velocity (PWV), and the augmentation index (AIx). In 14 healthy subjects, stimulation was done at the “heart” auricular point with a specialized be that was specially equipped with an electronic device to provide vibration at a frequency of about 30 Hz. The tests were conducted before during and after the manual acupressure and vibrational stimulation. The results of this study showed that the HR decreases ($P \leq 0.001$) and HRV total increased significantly ($P = 0.008$) during ear acupressure vibration and/or manual ear acupressure The pulse wave velocity between the bifurcation of the aorta and the aortic root was decreased and, after vibrational and manual acupressure at the "heart" auricular acupoint, the augmentation index immediately increases.. The researchers stated that ear acupressure can influence the autonomic nervous system and these ear stimulation methods could cause "measurable, reproducible physiological alterations, especially of HR, HRV, and blood pressure, as well as changes in the parameters of human arterial stiffness and wave reflection"(Gao et al., 2012). This study is important for this review because of the increased HRV and lowered heart rate indicates vagal activity. It is also interesting because it was one of the first to have a technique to study arterial stiffness and acupuncture. There are some limitations of this study such as the small subject size, and because of the difficulty identifying an ear placebo point for such investigations, there was no control group with a control acupuncture point. The study was stated as the first investigation of noninvasive parameters in humans using ear acupuncture-like stimulation. However, because of the limitation stated above the hypothesis for this study will require future investigation for verification. The difference between the vagal effect of using needles auricularly verses acupressure would also be an important matter for future research.

In addition to these studies, two other insomnia studies had some conclusive results regarding the sympathetic nervous system and auricular acupuncture. The Kung, Yang, Chiu, & Kuo study was to examine how the change in cardiac sympathovagal activity by auricular acupuncture (AA) therapy would be related to the change in self-reported insomnia in postmenopausal women. After 45 post-menopausal women received 4-week-treatment of auricular pressure therapy, there was a moderate correlation between a greater percentage change in Pittsburgh sleep quality index with both a greater percentage change in normalized low frequency (LF) power of HRV as well as a lower percentage change in high frequency (HF) power of heart rate variability (HRV) . These results suggest that auricular acupuncture therapy led to more parasympathetic and less sympathetic cardiac activities. Thus contributing to the improvement in these women of their postmenopausal insomnia. (Kung et al., 2011).

Wang et al. conducted the second study on auricular acupuncture on insomnia. This study also examined auricular acupressure's effect on heart rate (HR) and heart rate variability (HRV) in patients with chronic insomnia. Again, the auricular acupoint "Shenmen" was selected for acupressure stimulation. A seed with adhesive plaster was applied at "Shenmen" on the left ear. The auricular acupressure was performed for 30 pressure movements per 15 seconds. This procedure was done every 10 minutes, for a total of 3 times. The researchers concluded that HR significantly decreased during and after the acupressure treatment. However, they noted that the effect only appeared in the second phase of the acupressure (10 minutes after the first stimulation). The total HRV also showed a significant increase with stimulation but with no long-lasting effect (Wang et al., 2013).

Kung and colleagues study was a more interesting acupressure study because of the length of the treatment time. Most of the VNS studies found for this literature review have only had limited treatment times. Acupuncture is a medicine that is most often used over longer durations to achieve maximum effects. This study showed that a four week, daily stimulation time period produced vagal-induced physiological and psychological effects. There are some limitations to this study. The placebo effect of AA cannot be ruled out from this observational study, and this was a specific study on menopausal women, whose physiology and response could be different than an alternative population. However, the changes in HRV at resting before and after AA treatment can present as vagal modulation for the purpose of this review. The insomnia study with Wang and colleagues was overall a poor study for insomnia since there was no clinical outcome data HR and HRV data correlating to the effectiveness of treatment on patients' insomnia. Also, there was no control group, so without a sham point, there is no indication whether the effect was with a classically use acupoint or nonspecific effect. However, for this review, the HR and HRV data do indicate the ability of acupoints in the ear's concha having the ability to stimulate the ABVN for vagal modulation in the treatment of fear extinction.

The study by Shi et al. also monitored HRV while having acupuncture treatment – investigating the acceptability and the impact would be of providing continuous auricular electroacupuncture as an integrative therapy with conventional medications for patients with depression. This study was the first to use a miniaturized system to supply continuous electrical stimulation at an ear acupoint in patients suffering from depression. After just 24 hours of this continuous electrical stimulation, the study found that all clinical scores (HAM-A, AIS, HRSD) plus HRV improved significantly. The study documented that three days of auricular electroacupuncture can improve various aspects of quality of life significantly (Shi et al., 2013). More essential to this research paper it also highlighted the significant increase of HRV while having continual acupuncture treatment. This "P-stim" type devise could be an important adjunct in not only improving the fear extinction during exposure-based therapy but providing the patient with a way of continually modulating the HRV to maintain enhanced retention of the treatment. Of course, since this is another small study done over a short duration, further studies would be necessary to verify these results. Additionally, an RCT employing this or similar device along with CBT or other exposure-based therapy would be essential.

The 2010 study (Marca et al., 2010) used a three-armed randomized trial to evaluate the effects of electro-acupuncture on vagal activity. This study was small with fourteen healthy men from 20-40 years but did have good controls important for measuring the effects on the autonomic nervous system. They participated in four examinations in random order (without repeat): a condition with placebo, a control condition without intervention, as well as manual and electroacupuncture. Because of the neuroanatomical evidence of afferent vagal innervation, acupuncture was used in the ear concha. The experiment was partially blind, except the examiner was no longer blinded when they applied the needles with or without electrical stimulation but were instructed to behave identically as the other conditions. The examinations took place once a week with each examination lasting 90 min, which consisted of 30 min of habituation and baseline measurement, then 30 min of one of the 4 intervention and 25 min of postintervention. The final result, controlling many adverse effects, was that electroacupuncture but not manual acupuncture was found to have a positive effect on RSA_{TR}. Although a well thought out study with unique controls (pain-response, belief in acupuncture, placebo and time effect) there were some limitations, such as the small sample size, the lack of women participants, and only healthy non-medicated participants. The strengths of the trial were the three armed trial with a non-needle based sham and a dedicated time for calming vagal activity. The results demonstrate that auricular electroacupuncture might be used as “mildly invasive, preventive or adjuvant therapeutic treatment in clinical or subclinical populations or even a preventive intervention in healthy subjects” (Marca, et al., 2010). If electroacupuncture has a more significant effect than manual acupuncture alone it would present as more beneficial replication for a proposed tVNS protocol. More extensive studies would need to be done to confirm these findings.

Feng and al completed a new randomized control study (RCT) which was published in April 2019 which showed a positive result of transcutaneous electrical (body) acupuncture stimulation (TEAS) combined with cognitive behavior therapy (CBT). However, this study was included in this review only because of its novel approach of acupuncture stimulation combined with exposure-based CBT therapy – which could provide a valuable reference for setting up research study protocols for the use of auricular acupuncture with CBT.

Finally, even with the stated limitations, these narrative literature review results strongly recommend acupuncture point stimulation as VNS for fear extinction in PTSD as an integrative adjunct in exposure-based therapies. Furthermore, auricular acupuncture therapies in terms of frequency, duration, and intensity may hold the key to using non-invasive VNS therapies over other tVNS devices. A well developed, robust study with an integrative protocol is necessary to confirm this recommendation and thereby garner the support for widespread acceptance of this holistic PTSD therapy.

Table 5

Acupuncture and VNS Treatments, Frequency, Duration and VNS/Fear Extinction Result

Study	Treatment	Tx Stimulation	Tx Duration	Result (+/-)
Pena et al,, 2013	Animal -Surgical VNS Left Vagus Nerve	30s with CS .4 mA, 30 Hz Pulse width: 500 µs	1 day	+Fear extinction +Retention
Pena et al., 2014	Animal -Surgical VNS Left Vagus Nerve	30s with CS .4 mA, 30 Hz 500 µs	1 day	+Fear extinction +Retention
Noble et al, 2017	Animal -Surgical VNS Left Vagus Nerve	30s with CS .4 mA, 20 Hz 100 µs	5 days over 11 day period	+Fear extinction +Retention
Noble et al., 2018	Animal - Surgical VNS Left Vagus Nerve	30s with CS .4 mA, 20 Hz 100 µs	1 day	+Fear extinction +Retention
Burger et al., 2016	Auricular tVNS – Left concha	30s on/30s off .5mA, 25 Hz	1 day	+ Fear extinction -Retention
Burger et al., 2017	Auricular tVNS Left concha	30s on/30s off .2-.5mA, 25 Hz, 250 µs	1 day	+ Fear extinction -Retention
Burger et al., 2018	Auricular tVNS Left concha	30s on/30s off .5mA, 25Hz 250 µs	1 day	-Fear extinction +US expectancy
Lamb et al, 2017	Auricular tVNS Left auditory meatus and posterior tragus	With US 20Hz, 100us, 80% pain threshold	1 day	+ Fear extinction
Aria et al.,	Auricular Press Needles Pt: Shenmen, Point 0	Post-Op	1 day	+VNS (LF/HF ratio)
Gao et al.,	Acupressure Electrical Stim and Manual Electrical stim – pen Pt: Heart	30 s at 30Hz Or 30s pressure	1 30s treatment	+VNS (HR/HRV)

Kung et al.,	Acupressure Magnetic pellets/adhesive Pt: Shenmen, Heart, Kidney, Brainstem, Subcortex	Press every sec for 1 min before sleep	4 weeks	+VNS (HF, HRV) +Insomnia reduction
Wang et al.,	Acupressure Seed/adhesive Pt: Shenmen	Press 30x per 15s every 10min for total of 3x	1 treatment	+VNS -Retention
Shi et al.,	Electro-acupuncture Ultra-thin needles "P-stim" Pt: Shenmen, Small Intestine, Heart	1mA, 1 Hz, 15min on/off	3 days (constant)	+VNS +Anxiety reduction
Marca et al.,	Electro-acupuncture Manual acupuncture (.2 x15mm) Bilateral Concha	30 min at 10Hz intensity to pain threshold or 30min manual	4 afternoons	+VNS (RSATR) -VNS (HRV) with manual acu
Feng et al.,	Transcutaneous electrical acupuncture with CBT Adhesive Electro-pads Pt: P6	50 Hz, 50 µs min sensory threshold for 30s and then ramped off over the next 15s = active for a total of 45s	1 treatment a week for 12 weeks	+Increased Clinical Response Rate +Increased Remission Rate

Future Research Protocols:

It would be more consistent with the current tVNS studies for fear extinction in PTSD to have electric stimulation (Table 5). Yet the evidence suggests that auricular acupuncture, acupressure, and electroacupuncture all had a significant effect on the vagal modulation (Table 5). More studies would be needed to ascertain the full difference between electro and manual acupuncture and acupressure since all three methods are shown to be effective in stimulating a parasympathetic response through VNS. There is not enough information on the TEAS to be critical of the process, yet it seems "percutaneous" electro-acupuncture stimulation rather than "transcutaneous" could cause an even better polyvagal response. In a sham-controlled study, it was concluded by researchers that PENS, when used at 4 Hz frequency, was more effective than TENS in providing short-term pain relief and improved functionality in patients with sciatica. (Ghoname, et al., 1999). This too needs further studies to decide which system of treatment would offer the most effective treatment for extinction and retention. Another quantity to factor in the "AA with exposure-based therapy" design is the integrative nature of this protocol for long term treatment. In the United States, it is generally necessary for a licensed acupuncturist to do the insertion and removal of needles and, conversely, most acupuncturist would not be trained in the techniques of exposure therapy. Therefore, the ideal situation would be with an acupuncturist and psychotherapist to create a treatment situation where they could share space – with the acupuncture present in the building but only needed for the setup of the needles and removal and follow up treatments with these individuals. The benefit of his model is that the follow up could lead to even greater efficacy of treatment by focusing on other PTSD symptomology of the patient (insomnia, pain, anxiety, depression, etc) (Grant, et al., 2018). In some States, the therapist could be trained sufficiently in acupuncture technique, as is the case with the NADA protocol, to facilitate VNS during the exposure therapy. Although only one of the insomnia studies had a treatment protocol of over a week (Table 5), based on other successful acupuncture treatment research, a protocol that stacked multiple treatments in the first 4-6 weeks (2-3x a week) followed by weekly treatments for up to 12 weeks would be recommended. Protocols could include 2 AA points directly in the concha such as heart or lung as well as Shenmen. If electrical stimulation is incorporated, the VNS protocols suggest that a lower mA vs a high mA is not only more easily tolerated but has better results. Therefore, a range of .5-1 mA would be an effective starting point at an intensity below the pain threshold. Adding acupressure seeds between treatments should also add to improved overall symptoms. With that said, the results do show the effectiveness of auricular acupressure alone on vagal HRV, suggests that it could be used as a stand-alone method with exposure-base therapy. The availability of an acupressure electro-stimulator such as the "Pstim" or other units would be worth exploring. This could make the combination of acupuncture VNS and a CBT type therapy much more accessible. It would seem as far as physical stimulation is concerned that auricular acupuncture or electroacupuncture would be more effective. However, this is unknown in this context, and an RCT on the difference of effectiveness between auricular acupuncture and acupressure on vagal tone during fear extinction exercises are warranted.

CONCLUSION

This research paper was designed to bring attention to the effectiveness of auricular acupuncture to stimulate the vagus nerve for the treatment of fear extinction in PTSD. The review studies found do support the therapeutic effects of VNS and tVNS in conjunction with exposure-based therapy for the treatment of fear extinction. The research also indicates auricular acupuncture point stimulation's ability to modulate HR, HRV, and RSV, indicating it's VNS capabilities and capacity to be an effective adjunct therapy as VNS in the treatment of fear extinction in PTSD. Therefore this integrative approach of CBT combined with VNS through auricular acupuncture could become an inexpensive, non-invasive, and effective way to accelerate the treatment of the root of PTSD through improved fear consolidation.

More RCTs evaluating auricular acupuncture's effectiveness in an exposure-based therapy setting, as well as assessing the ratio efficacy/cost of auricular acupuncture stimulation versus other neurostimulation modalities are warranted. These studies could boost emerging vagal stimulation science used in combination with this known ancient technique – not only helpful for these PTSD therapeutic purposes but also for understanding human's ability to heal via vagus nerve modulation. Auricles, as Chinese Medicine has shown for thousands of years, might now become increasingly known as the "modern", most affordable, and effective gateway to health and healing.

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APPENDIX A

The Vagus Nerve:

The vagus nerve is the tenth cranial nerve and the longest nerve of the autonomic nervous system. This nerve supplies motor nerve impulses, receives sensory impulses, and visceral innervation. It modulates parasympathetic control of the lungs, heart, and gastrointestinal systems and has effects on blood vessels, sweat glands, smooth muscles, and the endocrine system (He et al., 2012).

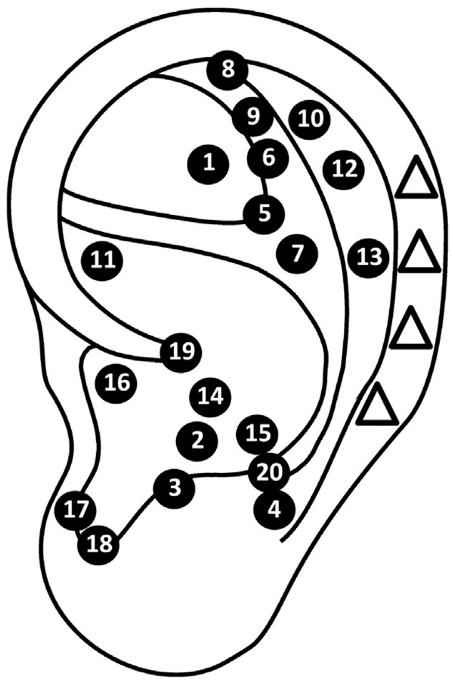
Illustration of Auricular Innervation (He et al. 2012):

"The innervations of the external auricle. The innervations of the auricular branch of the vagus nerve are marked by green color. The innervations of the auriculotemporal nerve are marked by red color. The innervations of the lesser occipital nerve are marked by blue color. The innervations of the greater auricular nerve are marked by yellow color". (He, et al., 2012)

APPENDIX B

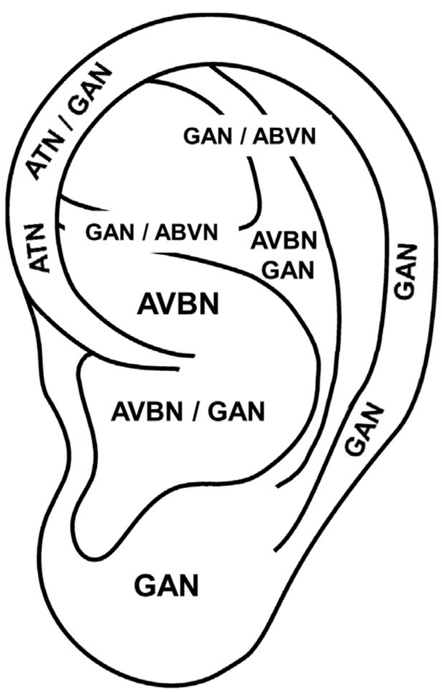
Auricular Acupuncture Points Illustrations from (Usichenko, Hacker, & Lotze, 2017)

A



A: "Auricular acupuncture (AA) points, used for treatment of patients with acute and chronic pain in randomized controlled trials (RCTs) included into meta-analysis of Asher et al., 2010. Black circles with numbers: various specific AA, the nomenclature is given in Table 1; triangles: non-acupuncture points for sham acupuncture on the helix of the auricle as a control condition in several RCTs from the meta-analysis." (Usichenko, Hacker, & Lotze, 2017)

B



B: "Anatomic map of afferent nerve supply according to Peuker and Filler, 2002, where cymba conchae is exclusively supplied by the auricular branch of the vagal nerve (ABVN)" (Usichenko, Hacker, & Lotze, 2017)

APPENDIX C

Auricular Vagal Afferent Pathway Illustration (He et al., 2012)

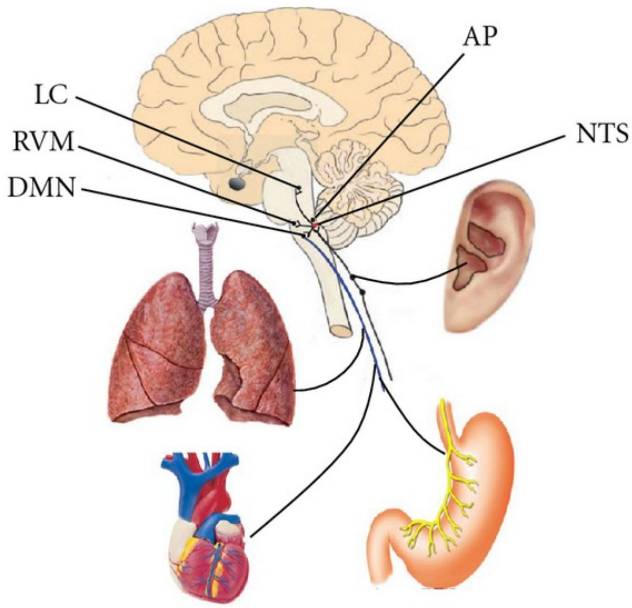


Figure 5: "Auriculovagal afferent pathway" "(AVAP): both the autonomic and the central nervous system could be modified by auricular vagal stimulation via projections from the ABVN at the auricular concha to the NTS.

NTS: nucleus of the solitary tract;

DMN: dorsal motor nucleus of the vagus;

AP: area postrema;

RVM: rostral ventrolateral medulla;

LC: locus coeruleus." (He et al., 2012)