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The Effects of Alpha Stimulation on Induced Anxiety

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ABSTRACT

Anxiety is defined as an emotional and physical reaction that prepares us to confront a feared stimulus. Among the many measureable changes induced by anxiety are changes in facial electromyography (EMG), heart rate (HR), and sweat gland activity (EDG). At a pathological level anxiety interferes with cognitive processes. Currently, when anxiety crosses into the pathological level, it is treated with a variety of therapies that share in their use of periods of exposure to anxiety-inducing stimuli. Several devices have been developed to alter brain activity by transcranial electrical stimulation (TCES). One such device, Alpha-Stim[®], has been shown to reduce anxiety in clinical samples. This suggests that the device might be useful in therapeutic exposure sessions, though no research to date has examined its use in such settings. In a double-blind, placebo controlled study participants were exposed to stimuli derived from the International Affective Picture System (IAPS) database that were chosen for their ability to elicit anxiety. A repeated measures analysis of variance was performed on recorded physiological data (EDG, HR, EMG) and subjective experience of anxiety as measured with Subjective Units of Distress Scale. Analysis of subjective units of distress scores showed that repeated exposure to anxiety eliciting pictures produced decreasing levels of distress over time ($F(1,13) = 5.831, p = .031$). EDG analysis revealed no statistically significant results. HR analysis revealed that TCES produced lower heart rates throughout the exposure (main effect of treatment; $F(1,12) = 120.907, p < .001$), and a trend toward increased heart rate during the exposure (treatment by time interaction; F

(1,12) = 3.514, $p = .085$). Frontalis EMG analysis revealed a trend for the treatment groups to differ in their experience of negative emotional valence over the course of the exposure ($F(1,12) = 3.209, p = .098$).

The Effects of Alpha Stimulation on Induced Anxiety

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CHAPTER I

INTRODUCTION

Exposure remains the most efficacious treatment for anxiety disorders. Yet being the most effective therapy does not mean it is appropriate for every individual. There are many reasons for this. Most importantly, some prospective patients may be unable to tolerate the distress provoked by exposure procedures. For these individuals, alternative forms of psychotherapy and pharmacotherapy exist that vary widely in effectiveness, tolerability, and risk of addiction. This thesis will examine the benefits of a relatively new form of adjunctive therapy, transcranial electrical stimulation, and its effects on healthy individuals during exposure to fear/anxiety producing stimuli.

Literature Review

According to the *Diagnostic and Statistical Manual of Mental Disorders V* anxiety is the apprehensive anticipation of future danger or misfortune accompanied by a feeling of worry or distress with a focus on internal or external danger. Often the individual's appraisal of danger and the experience of fear are out of proportion to the stimulus and cause interference with the normal brain processes required for psychological homeostasis (Gorman, 2004, p. 2). Researchers and clinicians define anxiety as a biological warning system that unites mental and physical reactions to potentially dangerous situations (Hoehn-Saric & McLeod, 2000). Regardless of which definition one chooses, anxiety exists as a state of negative emotional arousal expressed

physiologically in a variety of ways, including increases in facial muscle tension, heart rate, blood pressure, respiration, and sweat gland activity (Hoehn-Saric & McLeod, 2000; Ragsdale, Mitchell, Cassisi & Bedwell, 2013).

Most individuals experience anxiety upon presentation of a potentially threatening stimulus. In the United States one third of the population will meet the criteria for an anxiety disorder at some time in their lives (Biedel et al., 2014). The National Institute of Mental Health reports that 18.1% of all U.S. adults have experienced an anxiety related disorder in the past 12 months, and of these cases 28% (4.1% of the adult population) are severe. Although anxiety disorders are highly treatable, only about one-third of those suffering receive treatment (Wang et al., 2005). In 1999, a study commissioned by the Association for Depression and Anxiety Disorders, entitled “The Economic Burden of Anxiety Disorders,” and published in the *Journal of Clinical Psychiatry* concluded that anxiety disorders cost the economy \$42 billion a year, including \$22.84 billion for anxiety-related conditions that mimic physical illness. Furthermore, individuals suffering an anxiety disorder are three to five times more likely to go to the doctor and six times more likely to be hospitalized for psychiatric disorders than those who do not suffer from anxiety disorders.

Currently, DSM-V recognizes 10 distinct syndromes of pathological anxiety (American Psychiatric Association, 2013). Reliable methods have also been developed to induce and objectively measure anxiety in animals as well as humans. An examination of analogue studies yields 36 commonly accepted procedures for inducing and/or measuring anxiety in mice (Kumar, Bhat, and Kumar, 2013). In humans, anxiety induces cognitive, emotional and physiological changes that can be assessed using a variety of

methods. Physiological changes may be assessed by measuring autonomic arousal as indicated by increases in heart rate, blood pressure, sweat gland activity, and respiration or by using electromyogram to measure tension in muscles that are sensitive to negative emotional valence (Hoehn-Saric & McLeod, 2000). In addition to these physiological measurements of anxiety there exists a variety of subjective psychological instruments. Therrien and Hunsley (2011) compiled a list of 91 different anxiety instruments, among them the State Trait Anxiety Inventory, Hamilton Anxiety Rating Scale, Goldberg Anxiety and Depression Scale, General Health Questionnaire, Beck Anxiety Inventory, Brief Symptom Inventory, Penn State Worry Questionnaire, and the Symptom Checklist-90. While these instruments were designed and normed for adult populations between the ages of 18 and 60 years, research indicates that they possess clinical utility for older adults (age 60-100 years) as well. Children, on the other hand, as their experience of psychopathology is different and the nature of the developing brain limits communication and understanding of abstract and internal stimuli, require separate instruments such as State-Trait Anxiety Inventory for Children, Hospital Fears Rating Scale, Venham Picture Test, and Visual Analog Scale (Forester and Park, 2012).

Basic scientific research on anxiety and clinical research on patients with anxiety disorders have resulted in useful tools for the laboratory assessment of human anxiety. Conceptually, emotions are adaptive responses composed of cognitive, experiential, behavioral, and physiological reactions to environmental stimuli (Lench, Flores, and Bench, 2011). As such, emotions can be measured across a variety of dimensions. One simplified way of characterizing emotions is on the basis of valence and arousal. Direct measurement of the physiological indicators of valence and arousal in response to

experimentally induced emotion enables researchers to measure the magnitude and time course of emotional responses in a laboratory setting (Lench et al., 2011). Cognitive and physiological similarities, such as effects on memory, threat response, and expressions of negative valence and physiological arousal, make a distinction between anxiety and fear difficult, often resulting in the use of either term to identify similar constructs (Gorman, 2004).

Currently several methods exist to elicit anxiety, including pictures, music, film, and verbal emotional priming (Lench et al., 2011). The International Affective Picture System (IAPS) is a well-established and widely used source of such (visual) stimuli (Lang et al., 1997). It consists of sets of standardized visual stimuli that produce predictable emotional reactions with normative ratings for each slide. The IAPS has been used in a variety of procedures to assess various participants' subjective emotional experience of external stimuli. Its effectiveness has been confirmed with a wide variety of self-assessment procedures (Colden, Bruder, & Manstead, 2008), psychophysiological measures (Colden et al., 2008), and imaging techniques such as fMRI (Colden et al., 2008). Thus, in the current study, we use a combination of self-report measures, such as an anxiety inventory and Subjective Units of Distress Scale, and physiological measurements, such as facial electromyogram, heart rate, and skin conductance, to assess the time and course of emotional responses to repeated exposure to anxiety-inducing stimuli from the IAPS database.

The IAPS set of stimuli was chosen because of its similarity to exposure procedures used to treat anxiety. The gold standard for treatment of troublesome anxiety and anxiety disorders remains cognitive behavioral therapy. This family of therapies

consists of a variety of treatments used in isolation or in combination that include cognitive restructuring, exposure, problem solving, applied relaxation, and biofeedback (Cuijpers et al., 2014, p. 131). Of all these techniques exposure remains the most effective (Harned et al., 2014). This intervention involves systematically confronting feared stimuli in a safe and controlled manner so that maladaptive and false beliefs about danger are challenged and fear is reduced (McCann et al., 2014). For exposure therapy to work, the feared stimuli must be encountered repeatedly until the anxious arousal that accompanies the feared stimulus has abated. Several explanations exist as to why this technique is so effective. The Emotional Processing perspective holds that repeated systematic exposure to a feared stimulus exposes the full fear structure encompassing stimulus, response, and meaning elements. As this system is activated, usually indicated by increases in anxious arousal, new information incompatible to the client's fear structure is added and integrated (McCann et al., 2014).

Successful exposure interventions result in a reduction in anxiety after the participant experiences several exposures across multiple sessions. When conducting these procedures, client subjective perception of anxiety indicates to both the clinician and the client the amount of work that is needed. According to Craske et al. (2014), the inhibitory learning model of extinction is based on classical conditioning. This model posits that the exposure modifies the connection between the conditioned stimulus (CS) and the unconditioned stimulus (US). After a successful exposure, the link between CS-US is altered such that the CS now possesses an additional inhibitory meaning as well as the original excitatory meaning.

Regardless of perspective, the underlying mechanism remains that the individual learns that the fears that accompany the stimulus are irrational. This does not mean that the dangers of these stimuli do not exist, but that the individual's appraisal of the danger is inaccurate. In order to teach this lesson, exposure is provided by the clinician either covertly (via mental imagery) or in actuality (*in vivo*) and either gradually (*systematic desensitization*) or all at once (*flooding*). Despite the effectiveness of exposure as a treatment for anxiety, there are drawbacks. It has been argued by Harned et al. (2011, 2014) that, because exposure involves making the client confront a feared stimulus through compulsion, it is insensitive, contraindicated, potentially damaging, and perhaps even unethical.

In addition to the aversive nature of exposure therapies, questions remain regarding the generalization of exposure effects beyond the treatment environment. Because most exposure therapies are conducted in a safe environment under the supervision of a qualified professional, there exists the possibility that conditioning effects may be limited to this artificially controlled setting (Craske et al., 2014). Outside of the therapeutic context it is possible for the fear to return (i.e., that the extinction effects will be specific to the context in which the extinction trials occurred). In other words there exists a very real possibility that fears extinguished within the therapeutic context will not generalize to the client's personal environment. In addition as these treatments rely on learning, many individuals may not obtain clinically significant symptom relief or may experience a delayed return of their anxiety upon termination of therapy (Craske et al., 2014).

Other individuals experience levels of anxiety that cause them to fail to confront the underlying sources of their pathology. Once again Craske et al. (2014) argue that these individuals may not be able to effectively engage in extinction learning due to deficits that not only limit therapeutic engagement but may also have contributed to the original anxiety disorder. In simpler words some clients may just be too anxious to undergo exposure treatments. In these cases alternative treatments would include psychopharmacological methods, such as selective serotonin reuptake inhibitors (SSRIs) and benzodiazepines, which carry their own risks of side effects and misuse (Nutt, Ballenger, Sheehan, & Wittchen, 2002), and other forms of psychotherapy, which may cause excessive anxiety and be too costly and time consuming (Nutt et al., 2002).

Yet for all its potential shortcomings, exposure therapy remains the most effective way to treat anxiety disorders. And for the individuals for whom exposure does not quite fit, a relatively new device called an Alpha-Stim[®] exists. This device, when clipped to the earlobe, generates a low level electrical current across the cranium and has been shown in a variety of studies to reduce depression and anxiety. The use of this device during exposure techniques may serve to reduce more quickly the anxiety that accompanies the feared stimulus, and the portability of these devices may allow the therapist and client to take exposure therapies out of the therapist's office and into the client's natural environment. This might increase the likelihood that the exposure therapy would generalize to environments outside of the therapist's office.

Transcranial Electrical Stimulation

In 1979 the U.S. Food and Drug Administration approved the first transcranial electrical stimulation (TCES) devices for the treatment of insomnia, depression, and

anxiety. These devices provide noninvasive brain stimulation using pulsed, low amplitude electrical current applied to the head via electrodes placed on the ear lobes (Barclay & Barclay, 2014; D. Kirsch, personal communication, March 24, 2014). TCES was originally approved for the treatment of depression, anxiety, and insomnia (Barclay & Barclay, 2014; Kirsch & Nichols, 2013). Other studies have shown TCES to provide relief from chronic headaches, low back pain, and fibromyalgia (Lee et al., 2013). It has also been used to treat individuals with substance use disorders and withdrawal symptoms (Ehlers & Phillips, 2007). Kirsch (2002) identified 126 published studies involving 4,541 subjects, the majority of which showed TCES to be effective with few side effects. These studies have suggested that TCES is at least as effective as biofeedback and relaxation therapies in treating anxiety (Gibson & O'Hair, 1987), and superior to placebo in the treatment of insomnia (Bystritsky, Kerwin, & Feusner, 2008; Koleoso, Osinowo, & Akhigbe, 2013).

When the device is clipped to the earlobes, a low-level, 1 mA electrical pulse is transmitted across the head at 0.5 hertz, resulting in a resting, or alpha, state (Barclay & Barclay, 2014; D. Kirsch, personal communication, March 24, 2014). In this state brain activity, as measured by frequency of electroencephalographic tracings, lies between 13 and 30 Hz across both hemispheres (Kennerly, 2006). These frequencies are produced naturally in people who are drowsy or relaxed. Whether produced naturally or artificially, this is presumed to reduce stress, stabilize mood, and regulate awareness and perception of certain types of pain (Barclay & Barclay, 2014). Thus TCES is presumed to produce its effects by inducing changes in brain activity and stimulating the release of various neurotransmitters and endorphins (Zaghi, Acar, Hultgren, Paulo, & Fregni, 2009).

Research on TCES is relatively new. Because of this, researchers have not yet come to agreement regarding the exact mechanisms at work. Zaghi et al. (2009) question whether the current directly affects cortical neurons or whether the effect of stimulation is mediated by peripheral nerves. Some studies have shown that TCES alters the levels of various neurotransmitters in the brain (Ferdjallah et al., 1995; Liss & Liss, 1996; Shealy et al., 1998) and changes brainwave activity (Electromedical Products International, Inc., 2013; Kennerly, 2005). Briones and Rosenthal (1973) documented increases in 24 hour urinary free catecholamine in anxiety and asymptomatic patients who were exposed to TCES. Shealy et al. (1989) documented observable increases in brain levels of melatonin, serotonin, beta-endorphin and norepinephrine. Summarizing earlier research, Zaghi et al. (2009) concluded that the evidence was consistent with an association between cranially applied alternating current procedures and alterations in neurotransmitter release.

TCES provides an alternative to traditional pharmacological interventions. First line treatment for anxiety disorders includes selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), benzodiazepines, buspirone, and tricyclic antidepressants (TCAs) (Nutt et al., 2002). Compliance with treatment remains a problem as medication can sometimes cause adverse effects including weight gain, gastrointestinal and sexual difficulties, insomnia, and severe headaches (Rivas-Vasquez, 2001). These unintended consequences may often complicate compliance as they can be more unpleasant than the condition that they are designed to treat. In contrast, most studies on TCES have reported only rare and mild side effects. Moustafa et al. (2013) reported that the most common side effects found were headache (0.20%) and local skin irritation (0.11%). He also reported other adverse effects including

vertigo, dizziness, disorientation, seizures, nausea, and electrical skin burns at the site of the electrodes occurring very rarely. Many of these adverse effects can be modified by reduction in treatment intensity. An additional benefit is that, unlike pharmacological treatments, FDA approved TCES devices cannot be used for overdose or self-harm (Moustafa et al., 2013). Finally, the treatment itself is very cost effective. It generally consists of teaching the patient to operate the device at home and having their symptoms monitored by a licensed professional.

The Present Study

TCES has been examined with positive results in a number of studies, with a focus particularly on depression, anxiety, insomnia, pain, and substance withdrawal. In medical literature, TCES has been examined in clinics for its efficacy in the treatment of pain and anxiety for individuals in inpatient, outpatient, psychiatric, dental, and surgical settings (Kennerly, 2006). All of these studies have shown decreases in depression, anxiety, and pain in comparison to sham treatment groups. What has not been examined is the application of a TCES device in the setting of an individual undergoing exposure therapy.

Traditional exposure therapies require that a client experience both controlled distress induced by exposure to feared stimuli and a concurrent level of physiological arousal (Craske et al., 2004). This process allows the individual to reinterpret the relationship between the feared stimulus and physiological arousal. For some exposure methods, the individual undergoing treatment is taught relaxation skills to prepare for the feared stimulus. Like all skills these relaxation and breathing skills have to be taught and practiced before they can bring about any meaningful effect during treatment. And, as

previously mentioned, some therapists have ethical concerns about exposing clients to feared stimuli. What TCES represents in these cases is an opportunity to control the more unpleasant conditions of exposure therapy so that the client can undergo exposure in a relaxed/meditative state.

In light of the research indicating that this treatment is effective for chronic depression and anxiety, we test a TCES device called an Alpha-Stim[®] that is presumed to induce an alpha state in the brain. We use a randomized, double-blind placebo-controlled study design to evaluate the effect of this device when used as an adjunct to exposure treatment. So far studies of this and similar devices have focused on their use as a monotherapy for chronic depression, anxiety, pain, and the symptoms that accompany substance abuse withdrawal. No research has evaluated these devices for their ability to augment current recommended exposure therapies. Because fear and anxiety are so similar physiologically, this experiment examines TCES efficacy on reducing anxiety induced by exposure to stimuli derived from the IAPS database. It is hypothesized that exposure to anxiety provoking stimuli while under the influence of TCES will reduce the expected physiological anxiety response in normal volunteers.

CHAPTER II

METHOD

Design

The Alpha-Stim[®] device produces its effect in humans by passing a low-level electric current across the head by electrodes placed on the earlobes. The current study is a randomized, double blind, placebo controlled examination of the efficacy of the Alpha-Stim[®] device in reduction of anxiety when the participant is exposed to stimuli designed to illicit fear and anxiety. I hypothesize that application of the device during exposure of anxiety provoking stimuli will result in a decrease of anxiety.

Participants

Seventeen participants were recruited, screened and selected for inclusion in the present study. Subjects were drawn from the population of college students currently attending Abilene Christian University. Prior to any study-related activities, participants were presented with an informed consent document. They were allowed to read the document, ask questions about the study procedures, risks, and benefits, and were then asked to indicate their willingness to participate by signing the consent document.

Measurements

State Trait Anxiety Inventory

The State Trait Anxiety Inventory (Spielberger, 1968, 1977) is a 40-item scale that uses a 4-point Likert scale for each item and can be used to measure both trait anxiety (i.e., how a person experiences anxiety over time) and state anxiety (i.e., how a

person experiences anxiety in a given moment). The instrument is extensively used in both research and practice. Both subscales have been shown to be sensitive to experimental manipulation (Bieling et al., 1998). The instrument shows reliability coefficients (Cronbach's alphas) of 0.93 for trait subscale and 0.95 for the state subscale (Spielberger et al., 1970).

Subjective Units of Distress (SUDS)

In order to measure the participants' subjective feelings of distress, the participants were presented with a 100 millimeter line after each exposure, and asked to indicate, where on the line they felt their anxiety lay. The lines were marked at 0, 5 centimeters, and 10 centimeters for reference purposes.

Equipment

Physiological samples were collected using the BioPac MP 100 monitoring system, running Acknowledge 3.9 acquisition software. Two hundred samples per second were recorded from electrocardiogram, electrodermagram and facial electromyography channels. Electrocardiogram (ECG) signals were detected using standard snap connected Ag/AgCl electrodes placed directly on the skin in a modified lead II configuration, negative lead inferior to the right clavicle and positive lead inferior to the terminal rib at the left midaxillary line (Lobel, Granic, & Rutger, 2014). R-wave threshold was detected automatically and converted to beats per minute. Skin Conductance (EDG) signals were detected using BioPac TSD 203 transducers. Two Ag/AgCl 6 mm electrodes, housed in a non-polarizable polyurethane housing, were filled with isotonic electrode gel, and secured to the fingers of the participant's non-dominant hand between the interphalangeal joints of the first two fingers with velcro straps. Frontalis electromyogram recordings

were taken using two 8 mm Ag/AgCl electrodes secured horizontally at the midline of the participant's forehead (over the frontalis muscle, which elevates the eyebrow during expressions of negatively valenced emotions (Oberman, Winkelman, & Ramachandran, 2009). EMG data were reduced and rectified using a root mean square function averaging over thirty samples.

International Affective Picture System (IAPS)

The International Affective Picture System (Lang, 1997) is a database of pictures used for research on emotion and attention. IAPS was developed by the National Institute of Mental Health Center for Emotion and Attention at the University of Florida as standardized stimuli (Colden et al., 2008). It is comprised of 1,000 color pictures varying in emotional valence and arousal with content ranging from common, daily experiences (e.g., household items) to extreme emotional encounters (e.g., mutilated corpses). Twenty slides from the set were selected for their ability to reliably evoke fear and/or anxiety.

Procedure

Participants who met selection criteria were randomly assigned to placebo and experimental groups. Experimenters were blind to group membership. The State Trait Anxiety Inventory was administered, and one minute of base line physiological measurements was recorded. Next, conductive fluid was applied to the electrodes of the Alpha-Stim[®] device and the electrodes were attached to each earlobe. The settings for the device (experimental group: 100 mA; control group: off) were set by ACU Psychology Clinic staff trained to set up stimulus parameters according to each participant's randomization code. Both groups were then exposed to anxiety-eliciting stimuli derived

from the IAPS at a rate of one picture every 60 seconds. The entire exposure lasted 60 minutes (Electromedical Products International's, manufacturer of Alpha-Stim[®], recommended treatment duration). Participants had 3-minute physiological measurements taken at the beginning of the exposure, half-way through the exposure and at the end of the exposure session. A Subjective Units of Distress Scale (SUDS) was administered after each recording. Following completion of the exposure session, the State Trait Anxiety Inventory was administered again. A paired-sample student's *t*-test was performed on measures of state anxiety, and a repeated measures analysis of variance was performed to analyze data collected from the subjective units of distress scale and physiological measurements. With regards to the physiological measurements, for the sake of consistency, data were collected across the procedure; however, only the averages of the first and last collection periods were used for statistical analysis to assess change across the exposure period.

CHAPTER III

RESULTS

Of the 17 students that met selection criteria, 15 completed the experimental task and 2 dropped out. Of these 15 students, 14 were female. The group had a median age of 22 years with individual ages ranging from 18 to 50 years. The group included two Asian students, two African American students and two Hispanic students. The rest were Caucasian. Subjects were assigned randomly to treatment and control groups. Pre- and post-exposure anxiety levels were measured using the Spielberger State-Trait Anxiety Inventory (Form X). Analysis of paired student's *t*-tests revealed no change in state anxiety before or after the procedure ($t = -1.692, df = 14, p = .126$). Means are summarized in Table 1.

Table 1

State Trait Anxiety Inventory Form X

	<u>State Anxiety</u>		<u>Confidence Interval</u>	
	Pretest Mean (SD)	Posttest Mean (SD)	Pretest 95%	Posttest 95%
Placebo	31.5 (6.87)	34.62 (9.94)	25.76-37.24	26.31-42.93
Treatment	34.86 (6.01)	38.92 (9.1)	29.29-40.42	29.90-46.67



Figure 1. Mean Subjective Units of Distress (SUDS), taken after the first, second, and third exposures. Bars indicate standard error.

A SUDS was administered at three times during the exposure to assess the participants' subjective experience of exposure-related anxiety. A repeated measures analysis of variance was conducted to assess the effect of the procedure over time. Analysis of SUDS scores (Figure 1) showed a significant effect of time ($F(1,13) = 5.831$, $p = .031$ $\eta^2_{\text{partial}} = .310$) indicating that all subjects reported progressively less anxiety across the exposure procedure. However SUDS scores showed no significant effects of treatment ($F(1,13) = .019$ $p = .891$ $\eta^2_{\text{partial}} = .001$) or time by treatment interaction ($F(1,13) = .147$ $p = .147$ $\eta^2_{\text{partial}} = .011$).

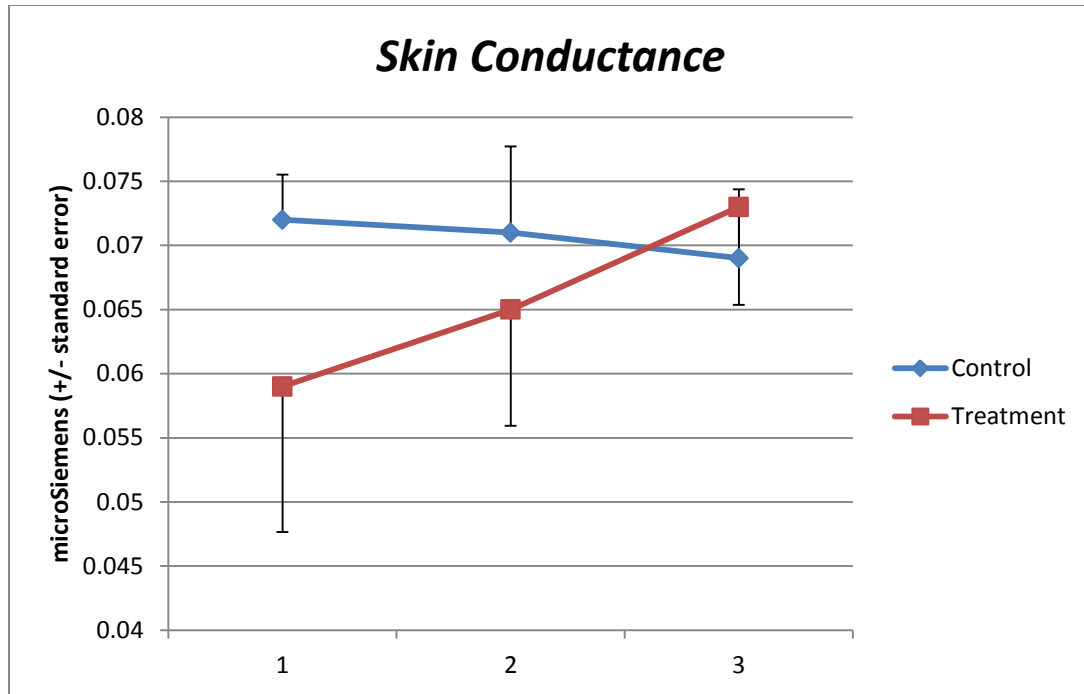


Figure 2. Mean SC comparisons (in microSiemens), taken after the first, second, and third exposures. Bars indicate standard error.

Physiological measurements of skin conductance, heart rate, and frontalis electromyogram were taken at 20-minute intervals during each exposure in order to measure the physiological expressions of anxiety induced by the exposure. It was hypothesized that these measures of arousal and negative emotional valence would decrease throughout the exposure as the participants habituated to the stimuli. It was further hypothesized that the treatment group would experience greater decreases in skin conductance (EDG), heart rate, and frontalis electromyogram (EMG) than the placebo group. Examination of EDG means (Figure 2) yielded no significant effect of treatment ($F(1,12) = .072$, $p = .793$, $\eta^2_{\text{partial}} = .006$), time ($F(1,12) = .019$, $p = .894$, $\eta^2_{\text{partial}} = .002$), or time \times treatment interaction ($F(1,12) = 2.883$, $p = .115$, $\eta^2_{\text{partial}} = .194$).

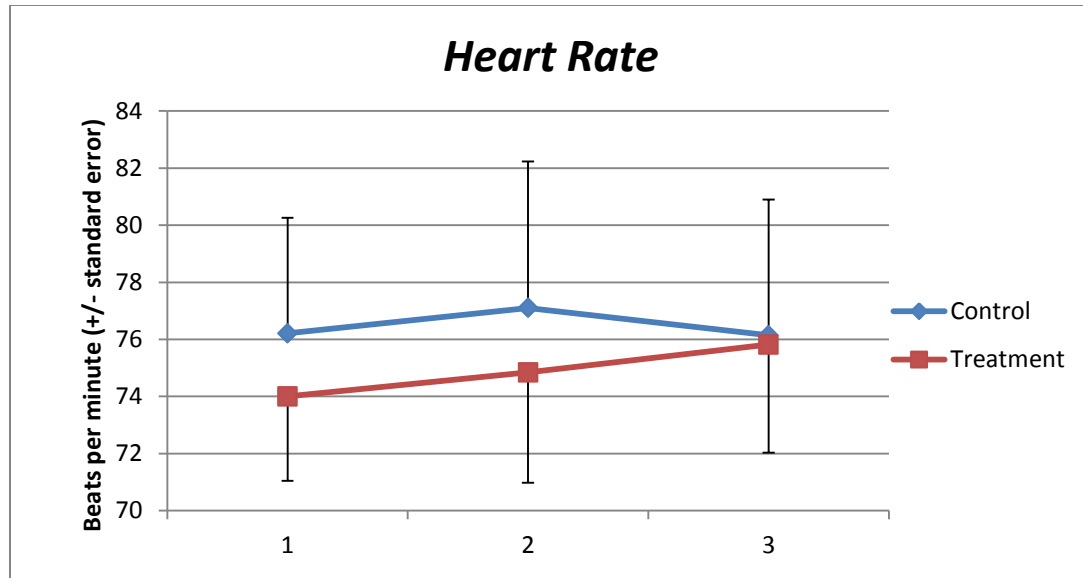


Figure 3. Mean heart rate (in beats per minute), taken after each exposure. Bars indicate standard error.

Analysis of heart rate activity (Figure 3) showed a significant effect of treatment with active treatment producing lower heart rates ($F(1,12) = 120.907$, $p < .001$, $\eta^2_{\text{partial}} = .910$), and a trend toward increased heart rate over time ($F(1,12) = 3.514$, $p = .085$, $\eta^2_{\text{partial}} = .227$), but no treatment x time interaction effects ($F(1,12) = .965$, $p = .345$, $\eta^2_{\text{partial}} = .074$). Means are summarized in Figure 3.

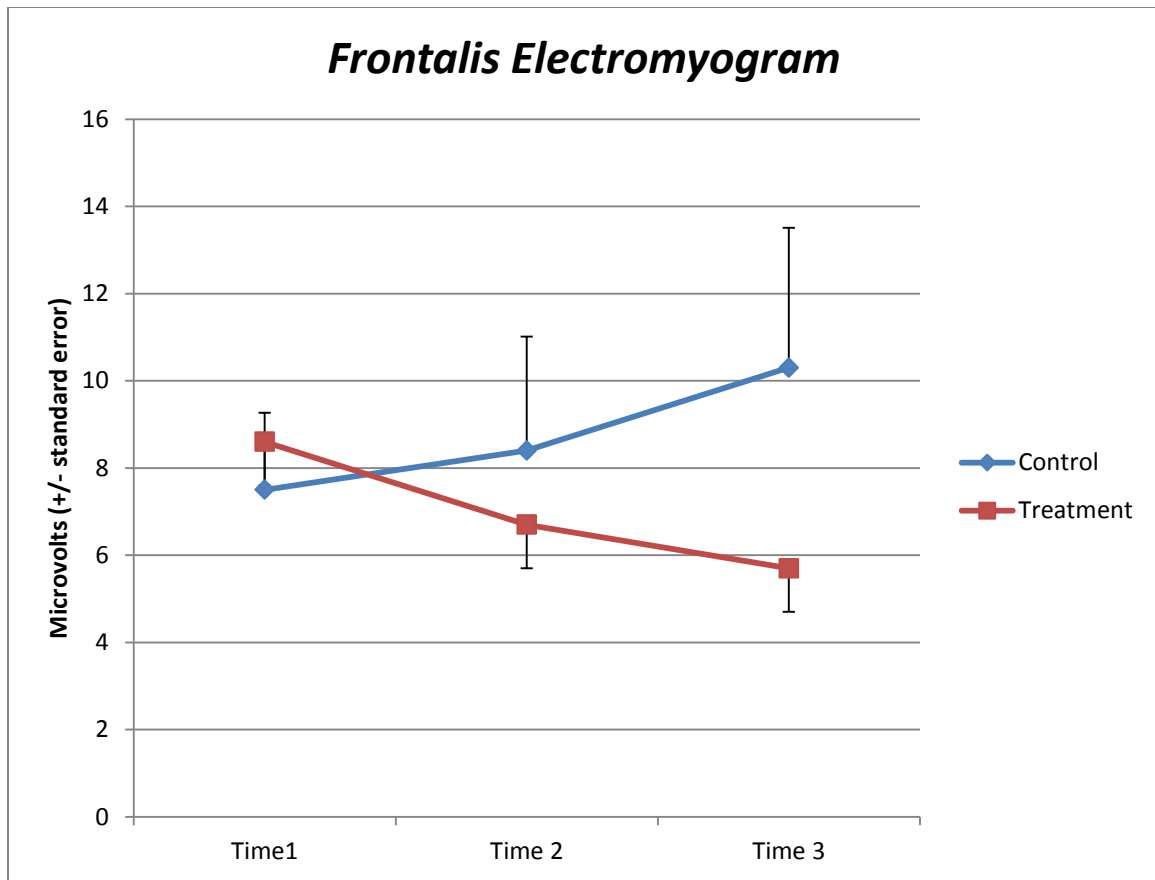


Figure 4. Mean EDG activity (in microVolts), captured after each exposure. Bars indicate standard error.

An analysis of frontalis EMG electrical activity (Figure 4) revealed no main effects of treatment ($F(1,12) = .228, p = .642 \eta^2_{\text{partial}} = .019$) or time ($F(1,12) = .526, p = .482 \eta^2_{\text{partial}} = .042$), but did show a trend for the treatment \times time interaction ($F(1,12) = 3.209, p = .098 \eta^2_{\text{partial}} = .211$). This trend is shown by the divergent directions of EMG change in the experimental and control groups. The control group showed an increase in EMG activity over time from 7.5 microvolts to 10.3 microvolts, while the treatment group showed a decrease in EMG activity from 8.6 microvolts to 5.7 microvolts.

In addition to these subjective and physiological measures, indicators of somnolence such as, rapidly blinking eyes, yawning, and head nodding were also observed during the experimental manipulation. These behaviors were observed in 4 of the 7 participants in the treatment condition and in only 1 of the 8 participants in the placebo condition. These treatment effects trended toward significance with a (one-tailed Fischer's exact value of 0.10).

CHAPTER IV

DISCUSSION

The purpose of this experiment was to evaluate the ability of a novel transcranial electrical stimulation device to facilitate exposure interventions by allowing for control over emotional arousal. It was hypothesized that all study subjects would show initial increases in physiological arousal and negative emotional valence when exposed to anxiety-inducing visual stimuli and that they would habituate to the stimuli as they were repeated. I also further hypothesized that transcranial electrical stimulation would produce faster habituation and less anxiety.

The experimental exposure procedure was designed to be analogous to clinical exposure procedures used in systematic desensitization. Notable differences in the experimental procedure include the use of a nonclinical sample and the use of standardized visual stimuli (IAPS) rather than subject-specific anxiety-inducing stimuli related to clinical anxiety states. The IAPS stimuli selected for this study were chosen because of their ability to induce negative emotional valence, physiological arousal, and subjective reports of increased anxiety in healthy adults (Colden et al., 2008). Individual pictures depicted a variety of scenes, from interpersonal violence to natural disasters.

Our study sample was almost uniformly female, a factor that limits general application of study findings. On the other hand, this may have reduced variability in our measurements since Barke, Stahl, and Kroner-Herwig (2012) found that women are more likely than men to rate stimuli as anxiety-producing.

Pretest and posttest anxiety were assessed using the Spielberger State Trait Anxiety Inventory Form X (Therrien & Hunsley, 2011). Pretest measures of anxiety showed normal levels of anxiety. Comparing pretest and posttest levels of state anxiety (Table 1) showed no effects of treatment, time, or their interaction. This demonstrates that the exposure procedure was well-tolerated by our subjects and did not induce unresolved anxiety. This lack of significant change in state anxiety before and after exposure could be due to one of two causes: the exposure did not induce anxiety-related distress or subjects habituated to the induced distress.

Examination of SUDS demonstrates the effectiveness of our experimental manipulation. Analysis of SUDS scores showed that subjects had elevated levels of distress early in the exposure period and that these levels decreased as the exposure period continued. This is the expected course of anxiety-related distress in an exposure session and is consistent with our first hypothesis. The absence of a treatment effect or treatment by time interaction shows that the transcranial electrical stimulation did not significantly affect subjective levels of distress or the speed at which habituation occurred. This might lead one to think that the electrical stimulation had no effect on the course of exposure; however, an examination of the physiological data yields a different picture.

Emotions are a complex combination of cognitions, autonomic responses, voluntary behaviors, and subjective feelings (Barke et al., 2012). When people experience anxiety, thought processes are focused on the threat stimulus (if known) or are used to identify a threat (if not known). Sympathetic nervous system activation leads to increased heart rate, increased blood pressure, pupillary dilation, and sweating; skeletal

muscles alter tension in preparation to respond to threat or to signal distress to others; and subjective experiences of desire to freeze, fight, or flee increase. Many of these anxiety-related responses can be measured physiologically and are useful in supplementing subjective reports of anxiety. In this study, we used three physiological measures to assess emotional changes in our subjects. One useful way to view emotions decomposes them into a combination of emotional valence (positive or negative) and physiological arousal (high or low). Using this model, anxiety is seen as a negative valence, high arousal state (Barke et al., 2012). As such, we chose to use galvanic skin conductance as a sensitive measure of arousal (Ragsdale et al., 2013), frontalis (the large muscle in the forehead) electromyographic activity as a sensitive measure of negative emotional valence, and heart rate as a mixed indicator of valence and arousal (Coan & Allen, 2007).

Normally, when a person is exposed to situations that elicit anxiety, the sympathetic nervous system responds by increasing its activity to the degree necessary to cope with the situation. This is also true when people with anxiety disorders are exposed to stimuli related to their pathology. However, when compared to a healthy population, individuals suffering from anxiety disorders frequently show smaller physiological responses and diminished physiological flexibility in response to anxiety-provoking stimuli not associated with their pathology as indicated by tension measured in the frontalis muscle (Hoehn-Saric & McLeod, 2000). In this experiment we were able to document small but consistent differences in arousal between placebo and treatment groups of healthy college students. We were also able to document divergent valence trends between treatment and placebo groups.

Overall, the data show that subjects in the treatment group were less physiologically aroused, especially early in the course of exposure, than the control group. This is seen in the significantly lower heart rate in Figure 3 and the trend in increased behaviors indicating somnolence in treatment group subjects. It is surprising that the skin conductance data did not reflect the change in arousal level, though the small sample sizes significantly limited the power to detect this effect.

Interestingly, the data also show a trend-level treatment by time interaction in frontalis EMG. This indicates that, while control subjects showed a gradual increase in their negative experience of the stimuli, those in the treatment group started out experiencing similar levels of negativity that decreased throughout the course of exposure. The strength of these findings is, of course, limited by low statistical power.

Taking the observed physiological responses and the SUDS data together, an interesting picture of the exposure session presents itself. While both groups of subjects showed increased distress at the beginning of the exposure session and habituated over the course of exposure, they had markedly different physiological responses to exposure. The control subjects maintained their arousal levels throughout exposure and increased their experience of negative valence over time. The subjects receiving active stimulation, on the other hand, showed physiological and behavioral evidence of low arousal, especially early in the exposure session with some evidence of increased arousal over time. This low, but increasing, level of arousal, however, was accompanied by a gradual decrease in the experience of negative valence.

The lower levels of physiological arousal seen in the subjects receiving active stimulation are consistent with the previously observed effects of TCES. The fact that this

decrease in physiological arousal did not affect the reported SUDS scores during exposure suggests that controlling arousal levels with TCES is unlikely to decrease the effectiveness of exposure in a therapeutic setting and may even be useful in improving the tolerability of exposure procedures for clients who would normally be too anxious.

Power in this experiment was a problem as we had only 15 subjects (8 placebo, 7 treatment), which hindered our ability to detect differences between groups. Observed power when testing for treatment effects on EDG revealed an η^2_{partial} value of .006. This value increased only slightly when looking for treatment by time interactions ($\eta^2_{\text{partial}} = .194$). As expected, as observed power increased so did significance. An examination of the EDG recordings in Figure 2 indicates that participants in the treatment condition had a lower skin conductance at first recording that increased to a level equivalent to that of the placebo condition at time three, while the placebo condition remained fairly stable. We suspect that low observed power in these cases hindered our ability to see significant changes more consistent with our hypothesis that the treatment group would show less arousal than the placebo group. EMG observed power was insufficient to detect the treatment effect at $\eta^2_{\text{partial}} = .019$ but was sufficient enough to detect the treatment by time effect at $\eta^2_{\text{partial}} = .211$.

Blinding in this experiment was also problematic as the TCES could sometimes be detected in the EMG recording. At times a distinct repeated pattern would be shown during an otherwise flat EMG recording; however, in order to preserve the blinding, no recording of this signal was made, nor was any alteration made in this experimental procedure, or the statistical analysis as we felt the effects on the collection would not be sufficient enough to warrant a change. In addition, one participant reported feeling a

slight pulse at the application site of the TCES device. This recollection is made entirely from memory, as no other participants reported feeling any similar effects. In order to preserve the blinding, this was also not recorded. These problems were encountered largely because the experiment team was working with an unfamiliar device. Because there was a significant amount of time between recording and analysis and these subjective reports were not recorded, we do not believe that there is sufficient reason to believe that blinding was significantly affected. However, in future research it would be prudent to have the device run by an individual who is not blinded and will not take part in the data analysis in order to ensure that the device is operating according to the recommended and experimental parameters. This individual would also serve another purpose. In addition to operating the device, he/she should also debrief the participant in order to insulate the investigator from commentary that may serve to bias the experimenter.

Another limitation of this study is that it uses healthy control subjects rather than clinically anxious subjects. This raises the possibility that the effects observed in this study may not generalize to the clinical population. As such I can see three possibilities; the first is that using transcranial electrical stimulation as an adjunct for exposure strategies can have an entirely different effect in a clinical population. Despite the fact that this device was developed and tested to treat conditions such as depression, anxiety, and insomnia, it is possible that it would not alter arousal levels sufficiently to be tolerated in a clinical population. A second possibility is that using the device could yield problems similar to that of current exposure therapies, limiting the generalization of exposure effects so that the exposure will not translate to conditions when the device is

not being worn. Third, the device could lower the perception of anxiety to the point where exposure is not effective.

The goal of exposure is to teach the client to tolerate the experience of negative emotions. Our examination of this device indicates that it may be useful in exposure procedures by allowing the therapist to control the experience of negative emotion making the exposure more tolerable. This experiment documents the ability of the Alpha-Stim TCES device to alter the emotional arousal and valence experienced during exposure to anxiety-provoking stimuli while preserving the expected habituation effects seen in the SUDS scores.

Even though this experiment was not conducted on a clinical population, examination of pre and post-test STAI mean scores indicated normal levels of anxiety. If a clinical sample of subjects with anxiety disorders showed a similar pattern of decreased arousal and negative valence during exposure while experiencing habituation to exposure related distress, this experiment would suggest that adjunct TCES would increase a participant's ability to tolerate therapeutic exposure sessions.

In summary, this research shows that TCES can decrease levels of arousal and negative valence induced by exposure to anxiety provoking stimuli without affecting the course of exposure as measured by SUDS. Because of problems of statistical power and external validity, it is important that further research be done on larger samples of clinical subjects to further examine the clinical utility of this device. Because of these drawbacks, it would seem that this device does warrant further testing in the exposure context, with a larger and clinical population.

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APPENDIX

IAPS STIMULI PRESENTED DURING THE EXPOSURE

The stimuli are listed in the same ascending order. The order is 1112, 1525, 1726, 2692, 3530, 3550, 5971, 5972, 6190, 6211, 6250, 6300, 6350, 6825, 6940, 9120, 9426, 9600, 9630. Pictures were assigned an additional number from 1-20 and then assigned a slot randomly, by use of a random number generator. No image was used more than once.



















