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An Evaluation of Anxiety Following Substance Abuse Withdrawal and Assessment of Somatic Treatments presently Available with a Focus on Cranial Electrotherapy Stimulation

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AN EVALUATION OF ANXIETY FOLLOWING SUBSTANCE ABUSE WITHDRAWAL AND ASSESSMENT OF SOMATIC TREATMENTS PRESENTLY AVAILABLE WITH A FOCUS ON CRANIAL ELECTROTHERAPY STIMULATION

by

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ABSTRACT

Addictive disorders/substance use disorders (SUDS) affect almost everyone in the United States, either directly or indirectly. The cost of substance abuse to the social and economic structure in the United States is huge. Anxiety is one of the most frequently mentioned symptoms which lead to relapse during the early weeks of recovery due to neurohormonal changes in the limbic system as well as cortisol production which occur during this time. Present research in the treatment of anxiety in substance abuse and long term recovery is focused on genetics and pharmaceuticals, however most pharmaceuticals produce sedation. Additional therapies in early recovery, which decrease the symptoms of anxiety while enhancing cognitive ability to learn and apply coping skills, are needed.

Purpose: The purpose of this dissertation was to identify the natural degradation of anxiety symptoms occurring during the first few weeks following detox from alcohol or opiates. To identify non pharmacological methods in use to decrease anxiety symptoms during this period, and then examine whether treatment with Cranial Electrotherapy Stimulation (CES) would enhance the degradation of anxiety symptoms.

Methods and Results: The initial prospective study of 53 men in residential treatment, measured anxiety on entry, 30 and 60 days. The results found that increased anxiety measured prior to a participant leaving against medical advice was more significant than increased anxiety measured on admission. The follow-on pilot study in the same residential program was a double-blind experimental study using CES with active and placebo CES units loaned from the manufacturer. The intervention was conducted during the first 3 weeks of opiate/alcohol abstinence; a period identified when anxiety peaks, and dropout rate is high. There were 29 men in the experimental

group and 31 in the placebo group. Salivary cortisol and state anxiety were measured on the first and final day of CES treatment. Anxiety was also measured at study enrollment and at 30 days when study enrollment was terminated. The results were statistically inconclusive as both the placebo and CES (experimental) groups trended downward; however the trend was greater in the CES group.

Discussion/Implications: Anxiety was identified as a significant factor in leaving treatment early. Cranial Electrotherapy Stimulation appears to decrease anxiety in non-substance abusing populations. However, these finding were not supported in this substance abusing population during the first month of recovery. Although CES appeared to be the most promising alternative therapy, more research is needed in the use of this and other emerging therapies for the treatment of anxiety symptoms during this early recovery period.

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CHAPTER 1: INTRODUCTION

Addictive disorders/substance use disorders (SUDS) affect almost everyone in the United States, either directly through a family member, or indirectly through friends or acquaintances. The cost of substance abuse to the social and economic structure in the United States is huge. Indeed, more than $.5 trillion is spent annually in healthcare, and associated crime or accidents (National Institute of Drug Abuse [NIDA], 2012). The personal cost to individuals is enormous, ultimately affecting all dimensions of functioning, including poor health (Curtis, Zahs, & Kovacs, 2013), poor interpersonal relationships, job losses, difficulty in school, as well as financial or legal problems (Harris, Smock, & Tabor Wilkes, 2011). Entering and maintaining recovery is a personal and ongoing struggle for most substance abusers. The treatment of substance abuse is complex and long term with no single effective treatment modality and involves collaboration between medical, psychiatric and social services.

The focus of this dissertation is gaining a better understanding of anxiety symptoms in the first few weeks following substance withdrawal in patients suffering from alcohol and opiate dependence. The aim of this research is to identify whether complementary and alternative therapies and cranial electrotherapy stimulation (CES) in particular, has a role in the treatment of anxiety symptoms during this period of early drug abuse recovery.

Addiction is a brain disease, which has been aptly described by Nora Volkow, Director of NIDA, as ‘’the brain being hijacked’’ (Volkow, 2014). Youthful experimentation or adult substance use to deal with stress, anxiety or pain (both emotional and physical) may lead to physical and psychological dependence. The trajectory from use to abuse, and ultimate dependence on one or more drugs, is due to a variety of physiological factors which are

influenced by the individual's genetic makeup and by life experiences which lead to changes in the gene alleles (epigenetic changes). Most individuals never become physically or psychologically dependent. However in those that are affected, the dependence may happen with the first use, or develop slowly over a number of years. Most do not recognize their drug dependence as a problem until it starts to affect personal, social, work and family relationships. What is initially seen as a solution to life stressors ultimately becomes the stressor itself.

The Stages of Change Model as described by Prochaska and DiClemente (1984) has become the working model for identifying substance abuse and starting treatment for the substance abuser. Motivational interviewing is used to move an individual from pre-contemplation to contemplating change in the substance abuse behavior. However, once the individual has made a decision to change, and moves from the preparation phase into the action phase, multiple obstacles line his path. Not all individuals need a medical detox but for those who do, protocols and treatment are available and easily implemented. The hard work starts after this, with the development of post-acute withdrawal symptoms which may be both physical and emotional. This is early recovery. Anxiety is one of the most frequently mentioned symptoms which lead to relapse during the early weeks of recovery (Levy, 2008) and is thought to be exacerbated by the disequilibrium of dopamine and endogenous opioids within the limbic system (Sher, 2002) as well as changes in the production of cortisol (Lovallo, 2006).

There is no single overarching theory which binds all the components of substance abuse. Many theories have been developed by individuals (or scientists) within the healthcare disciplines involved in the care and treatment of substance abusers. However, the Theory of Allostasis is broad enough to address the biopsychosocial dimensions of this multifaceted

disorder. Allostasis is conceptualized as a process that allows for ongoing evaluation and neurochemical adjustments between internal and external psychological demands on the individual (Ganzel, Morris, & Wethington, 2010). Allostasis is a central nervous system driven response which integrates appraisal, coping, learning and memory into the physiological response to these demands. Cortisol is produced when allostasis is not achieved and is a response to fear.

In the substance abuser, allostatic accommodation occurs initially within the neural circuitry of the limbic system in response to the drug of abuse, creating a drug dependent state of allostasis. When the drug of abuse is withdrawn, allostasis is lost and there is a further dysregulation of cortisol production (Koob, 2003) and therefore increased symptoms of anxiety.

Present research in the treatment of anxiety in substance abuse and long term recovery is focused on genetics and pharmaceuticals. The goals of most research are to reverse epigenetic changes associated with continued substance abuse, block negative memories and fully map the relationships of drugs to the limbic system (Nestler, 2014).

Group and individual psychotherapy has been the mainstay of substance abuse recovery for many years. Epigenetic changes occurring during psychotherapy are well documented (Feinstein & Church, 2010). Pharmacological agents presently used to attenuate symptoms of anxiety during withdrawal often have side effects which limit the efficacy of treatment, and in the recovery period, often are not used long term due to cost and limited effectiveness. Treatment with somatic and complementary methods (CAM) has been used in an adjunct capacity for many years in substance abuse and offers potential long term options.

The current state of the science of non-pharmacological therapies used for the treatment of the symptoms associated with anxiety during substance abuse withdrawal is discussed in Chapter 2 of this dissertation. Specifically discussed are somatic and complementary therapies (CAM) as used in the various Stages of Change Model (Prochaska & DiClemente,1984) within the continuum of substance abuse treatment. These therapies include acupuncture, massage therapy, meditation, yoga and music. Also identified are somatic therapies involving electrical and magnetic stimulation of neurons in the limbic system which have emerged as potential treatments for substance use disorders and the associated negative symptoms such as anxiety. These modalities include deep brain stimulation, transcranial magnetic stimulation, direct current stimulation and cranial electrotherapy stimulation (CES). Case studies with good results using these modalities have provided the impetus for further research into their effects on substance abuse and associated anxiety symptoms. However, the research is not broad with a limited number of studies completed.

In chapter 4 of this dissertation a study completed prior to the CES study discussed in Chapter 3, is presented. The use of present 'standard of care' treatment and subsequent changes in anxiety was examined during a single group repeated measures study of anxiety during the first two months of substance abuse treatment of men in the same treatment facility. Results in this study identified that anxiety is a significant factor in relapse during the first two months of treatment and that individuals with persistent anxiety were less likely to complete treatment than those whose anxiety remitted during the first few weeks after detox.

Decreasing the anxiety associated with post-acute withdrawal, is one of the components critical to insuring that patients continue on the recovery path. In Chapter 3, a Randomized

Controlled Trial (RCT) using CES conducted during the second to fourth weeks following detox is reported. This research was conducted with a group of 56 men in a residential treatment facility that had recently completed a medical detox from either alcohol or opiates. Anxiety and cortisol responses were measured during the treatment phase. Cranial electrotherapy stimulation (CES) is a somatic treatment that has been used for many years in the treatment of generalized anxiety and was identified as a modality which could be easily used in a recovery program with minimal training of both staff and patients. No recent studies have been reported on its use in decreasing anxiety in early substance abuse recovery. Although CES may be effective in reducing anxiety and cortisol response in this population, it was not demonstrated in this study. Psychopharmacological medications as well as placebo effect may have confounded the results.

The research results in this dissertation have extended the knowledge of the effect of anxiety symptoms on treatment dropout. This research also identified an alternative therapy in CES which may be effective in decreasing anxiety in early recovery in specific substance abusing populations. However further research is needed in the use of CES to identify whether higher anxiety at intake and earlier use of CES in opiate abusers would cause greater symptom attenuation. Recommendations regarding focus of treatment for anxiety were made based on the results of these studies and are being implemented in the residential facility where the research was conducted.

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CHAPTER 2: THE ROLE OF COMPLEMENTARY AND ALTERNATIVE THERAPIES IN SUBSTANCE ABUSE RECOVERY: A STATE OF THE SCIENCE PAPER

Psychotherapy and 12 step programs have been the cornerstone for substance abuse treatment for the last 75 years. Since the 1960s, substance abuse has slowly moved from being viewed as a moral failing to being recognized as a disease with a physiologic basis. As such, research in treatment has gradually moved the treatment focus to pharmacological solutions. Although progress is being made in identifying pharmacologic treatments for detox and recovery, attaining and sustaining recovery from substances of abuse remains a challenge, with many persons relapsing within 2 weeks of detoxification (Chutuape, Jasinski, Fingerhood, & Stitzer, 2001) and less than 50% remaining in recovery at 6 months (Gil-Rivas, Prause, & Grella, 2009). In fact, little improvement has been noted since the 1980s in achieving sustained recovery (Dennis, Foss & Scott 2007).

During these and subsequent years, there has been a renewed interest in all alternative and complimentary modalities as potential tools for decreasing symptoms associated with substance withdrawal, as well as increasing time in recovery. Acupuncture, massage therapy, yoga, meditation, exercise and music are often integrated into substance abuse treatment. Other emerging modalities involving somatic interventions include Transracial Magnetic Stimulation (rTMS), Deep Brain Stimulation (DBS), Direct Current Stimulation (DCS), and Cranial Electrotherapy Stimulation (CES). These are presently used to treat mood disorders and may also have a role in substance abuse treatment. The purpose of this state of the science paper is to explore the current research and use of complementary and alternative therapies (CAM) as well

as other non-pharmacological somatic modalities which may have a role in decreasing anxiety in substance abuse recovery treatment.

Scope of the Problem

Long term recovery from substance abuse is often an elusive goal for many people. The cost of abuse, detox, recovery and relapse is a financial burden to our society ((National Institute of Drug Abuse [NIDA], 2012) as well as to families and individuals struggling with substance abuse.

The burden of substance abuse often starts with youthful experimentation, early addiction and often accidental death. Substance abuse often stems from traumatic childhood experiences and mental health disorders, precipitated by genetic vulnerability (McQuown &.Wood, 2010). This vulnerability may be either enhanced by nature (genetic) or nurture (epigenetic) as has been described by social and biological scientists (Feinstein & Church, 2010; Nestler, 2014). This genetic effect continues into adulthood and often into the work environment. It is manifested by the negative consequences related to substance abuse which may include poor health, poor interpersonal relationships, job losses, difficulty in school, and financial or legal problems (Harris, Smock, & Tabor-Wilkes, 2011). Most individuals with substance use disorders experience some of these problems during their time in active addiction.

Adults in the prime of life often use opiates to cope with chronic pain. Alcohol and cannabis have been used for millennia to cope with stress and anxiety. Many persons become marginalized in our society as the substance of abuse affects their social and work lives (Darke, 2012). Substance abuse is a complex issue. The genetic influence of substance abuse extends far beyond the direct effect of the drug on the affected neurotransmitter and the up or down

regulation at the neuronal synapses (Solinas, Thiriet, Chauvet, & Jaber, 2010). Epigenetic changes associated with alcohol abuse are implicated in the attenuated immune response as is found in chronic inflammation and delayed response to infection. This is manifested in higher rates of pneumonia, hepatitis C progression and liver cancer, as well as affecting the health of many other organ systems within the body. (Curtis, Zahs, & Kovacs, 2013).

Not even our elderly are spared the effects of substance abuse, struggles with recovery and subsequent relapse. Alcohol abuse has long been recognized as increasing with aging and at retirement (CSAT, TIP #26, 1998). It is often in this later phase of life that alcohol abuse is identified by family members as being problematic, interfering with social and family life. Opiate use for non-medical and non-cancerous pain also increases in older adults (NSDUH, 2009). The elderly with substance use disorders are also more likely to have co-morbid psychiatric conditions and generally be in poorer health (Taylor & Grossberg, 2012).

Present Best Practices

The most successful model for substance abuse recovery in the past 75 years has been Alcoholics Anonymous (AA), or some variation of the 12 step program (Kaskutas, 2009). Used in many recovery programs as well as in the community, AA is useful for many substance abusers and is widely accessible (Miller, Sorensen, Selzer, & Brigham, 2006). However, it is not an effective model for all people as long-term recovery remains elusive for many (Dennis et al., 2007). Other individual and group psychotherapy treatments are also effective in decreasing the incidence of relapse (Finnerty, 2012), especially when used in conjunction with pharmacological treatment.

Medical management tends to be short-term and often not sustainable due to cost and intensity of management both by participants and the health care system. This is evidenced by the high percentage of individuals who cycle through substance abuse treatment and mental health facilities on a continual basis (Finnerty, 2012). Long term medical (pharmaceutical) management of substance abuse is limited to opiate replacement therapies such as methadone or buprenorphine maintenance. Many people also cycle in and out of these highly intensive and costly programs. The use of disulfiram, acamprosate and naltrexone in alcohol recovery is often limited to weeks or months (Seneviratne, & Johnson, 2015), and without supportive care has very little impact on length of recovery.

Over the past 2 decades, addiction research has focused on both neurochemicals and genetics. The role of genetics and the hypothetical ability for the reversal of epigenetic changes has become a primary focus for further research in sustaining substance abuse recovery (Nestler, 2014). The other focus at present is through pharmacological advances. However, counseling and behavioral change strategies also have a known long term impact on sustained recovery and gene reversal (Carroll & Rounsaville, 2007; Feinstein & Church, 2010). The emerging modalities involving the somatic interventions of Transcranial Magnetic Stimulation (rTMS), Deep Brain Stimulation (DBS), Direct Current Stimulation (DCS), and Cranial Electrotherapy Stimulation (CES), are presently used to treat mood disorders (Rosa & Lisanby, 2012), and may also have a role in substance abuse treatment. Other Complementary and Alternative Medicine (CAM) somatic therapies also have an adjunct role in substance abuse recovery.

A literature search was conducted using EBSCO and PSYCINFO. Only articles written in English were reviewed and were limited to studies published since 1980. Key words included

substance abuse, anxiety and each of the identified treatment modalities. One thousand and nine abstracts were reviewed and the results of thirty studies were included in this review. This review includes seminal studies when identified and systematic reviews when available. Studies with similar methods and outcomes were not included (See Table 1).

Table 1: Measures and results for CAM studies

Reference	Population	Sample Size	Study Type	Length of study	Measures	Outcome
Acupuncture						
Alster 2010	recovery program	100	Qualitative	1 year: 3-6 treatments	Interview post treatment	Improved anxiety
Bergdahl et al 2014	Residential early treatment	15	Qualitative	Unknown	Post treatment interview	Decrease in anxiety during treatment
Bearn et al 2009	During opiate detox	83	RCT (2 groups) acupuncture and TAU control	14 days	SOWS	No difference between groups
Black et al 2011	Early withdrawal	101	RCT (3 groups) Acupuncture, sham and relaxation	3 treatments over 2 weeks	STAI	Decrease in anxiety in all groups
Chang et al 2014	Veterans in recovery	67	RCT (3 groups) Acupuncture , relaxation and TAU	10 weeks 2 acupuncture sessions weekly	STAI	Decreased anxiety in both treatment groups
Massage, meditation and Yoga/mindfulness						
Alterman et al 2004	Recovery program	31	Qualitative (Mindfulness)	5 months	Pre post test ASI	No better than TAU

Reference	Population	Sample Size	Study Type	Length of study	Measures	Outcome
Black et al 2010	Recovery program	40	RCT (2-groups) Chair massage and relaxation	3 days	STAI	State anxiety sustained for 24 hours in CM group
Chang et al 2014	Veterans in recovery	67	RCT (3-groups) (relaxation, acupuncture and TAU	10 weeks 45 mins per week of relaxation therapy	STAI	Decreased anxiety after 2 weeks in treatment groups
Chen et al 2010	Substance abuse recovery	248	RCT (2 group)meditation/yoga vs relaxation	2 weeks	STAI	Decreased anxiety after 2 weeks both groups
Ospina et al 2008	All CAM in recovery		Systematic review 400 RCTs	various	various	Studies generally weak
Reader et al 2005	Alcohol withdrawal	50	RCT (2 group) Massage therapy and TAU	1st 4 days of Alcohol withdrawal	AWS	Decreased pulse after 15 minutes
Khanna et al 2013	Preparation Phase for Substance abuse treatment		Qualitative review	Various	Various	Improvement in stress symptoms. Decrease in sympathetic activity
Smith et al 2011	Community Volunteers	50	RCT (2 group) Mindfulness Stress reduction and Cognitive Behavioral Stress Reduction	8 weeks	Perceived Stress Scale – pre and post tx	MBSR p< 0.000 and CBSR p <0.013
Music Therapy						
Bonny 1986	Substance abuse	unknown	Qualitative			Evokes emotions and physiological response
Chaieb et al 2015	Various	30 articles	Qualitative review (binaural beats)	various	various	Modulating mood states with regular sessions
Mays et al 2008	Substance abuse treatment	unknown	Qualitative review Of 5 studies	Adjunctive therapy	interview	Felt was “helpful”
Trans cranial Magnetic Stimulation						

Reference	Population	Sample Size	Study Type	Length of study	Measures	Outcome
Gorelick et al 2014	Substance abuse treatment	316	Systematic review 19 studies	DLPFC per protocol	Interview, VAS	May be promising to decrease craving
Grall-Bronec et al 2014	Substance abuse treatment		Systematic review 18 studies	DLPFC per protocol	VAS	11 studies supported decreased craving
Mishra et al 2010	Alcohol dependence	45	RCT Single blind with placebo group	R DLPFC per protocol 10 sessions	ACQ-NOW, pre post and 1 month	Measured craving only Significant decrease
Mishra et al 2015	Alcohol dependence	40	RCT double blind to R and L DLPFC	Per protocol 10 sessions	ACQ-NOW Same time points	No difference between groups. Craving decrease significant
Jansen et al 2013	Substance abuse. Active users		Systematic review 9 RCTs. Placebo controlled. 3 with Alcohol	Various R or L DLPRC	Various	Decrease craving for alcohol in active group
Transcranial Direct Current Stimulation						
Jansen et al 2013	Substance abusers		Systematic review 8 RCTs TMS with DCS	Various	Various	Decrease craving in both groups
Cranial Electrotherapy Stimulation						
Bystritsky et al 2008	Generalized anxiety in outpatient	12	Open label	6 weeks	HAM-A	50% with decrease in anxiety
Barclay et al 2014	Anxiety in Primary care	115	RCT double blinded	5 weeks	HAM-A	85% with decrease in anxiety
Reference	**Population**	**Sample Size**	**Study Type**	**Length of study**	**Measures**	**Outcome**

Kirsh et al 2007	Substance abusers	335	Meta analysis 15 studies	various	various	Decrease in anxiety
Krupitsky et al 1991	Alcohol withdrawal	20	RCT		STAI	Robust Decrease in anxiety
Overcash et al 1989	THC withdrawal	32	Open label			Robust decrease in anxiety
Rose et al 2009	Caregivers of Alzheimers patients	42	RCT Double blind	30 days	Ham-A	No change in symptoms
Schmitt et al 1986	Polysubstance abuse in treatment	60	RCT double blind		STAI	Robust decrease in anxiety
Winick 1999	Dental office During procedure	33	RCT Double blind – placebo and CES	Single treatment	VAS at 3 time points	Significant decrease in anxiety

Complementary and Alternative Medicine

Acupuncture

Acupuncture has been used as a modality for the treatment of multiple conditions in China for several thousand years (Myatt, 2005). It is believed that endogenous opioids play a role in acupuncture analgesia and are released during acupuncture. Acupuncture is also thought to stimulate the hypothalamus and pituitary, resulting in a broad spectrum of neurotransmitter and neurohormone release; most importantly, the endogenous opioids and subsequent cascade to release of ACTH and then cortisol release (Lui, Li, Xia, & Terplan, 2009). This is conceptually similar to the gate theory of pain which was first described by Melzack and Wall (1965). The NIH Consensus Statement on Acupuncture (1997) advised that "there is sufficient evidence of

acupuncture's value to expand its use into conventional medicine and to encourage further studies of its physiology and clinical value" (Conclusion section, para. 5).

The NIH Consensus Statement (1997) also discussed multiple other factors that make research studies on the use of acupuncture difficult as many other factors may profoundly affect the therapeutic outcome. These variables are described as the relationship between the patient and the clinician, the amount of trust developed in the relationship, the expectations of both the patient and the clinician, as well as the belief systems of both individuals. These variables set the tone for the therapeutic relationship and contribute to the outcome of the (acupuncture) treatment (NIH, 1997). These same psychosocial parameters which affect treatment outcomes in acupuncture also affect outcomes in substance abuse treatment. Indeed, acupuncture has been used successfully in substance abuse treatment for more than 35 years (Cai-Lian, Liu-Zhen, & Fei, 2008). This is consistent with the NIH Consensus Statement (1997).

Most recent studies have focused on auricular acupuncture using a protocol developed by the National Acupuncture Detoxification Association (NADA). This protocol, using 5 needles placed at specific points in the ear auricle, is thought to improve retention in treatment by decreasing drug cravings, anxiety and lessening physical symptoms of withdrawal (Carter & Olshan-Perlmutter, 2014). However, research regarding the use of auricular acupuncture in substance abuse treatment, remains limited without clear outcomes in many studies.

Chang and Sommers (2014) reported on a study where auricular acupuncture was compared to relaxation response in a 10 week study on reducing craving and anxiety in veterans recovering from substance abuse. Results indicated substantial decreases in anxiety and craving following an individual session of acupuncture ($p < .001$) or relaxation response ($p < .03$), with craving

continuing to drop with continued sessions. However, it was not determined whether it was the regular attendance or daily practice of relaxation response techniques that elicited the change (Chang & Sommers, 2014). Similar concerns have been voiced by other researchers (Alster, 2010; Bergdahl, Berman, & Haglund, 2014).

In another recent Randomized Controlled Study (RCT) of 101 patients in substance abuse treatment (Black, Carey, Webber, Neish, & Gilbert, 2011), the hypothesis that auricular acupuncture would be effective in reducing anxiety was not supported. Anxiety was measured using a pre and post-test design. Participants were randomized into 3 groups: active auricular acupuncture using the NADA protocol, sham acupuncture, and relaxation therapy. Each received 3 treatments over 2 weeks. There was a significant drop in state anxiety in all treatment groups ($p<.001$) immediately following each treatment but there was no difference between each of the groups.

When auricular acupuncture was used during a 14 day opiate detox using methadone, auricular acupuncture was not found to decrease opiate withdrawal symptoms in a study of 83 participants (Bearn et al., 2009). In this RCT, participants were randomized into control and acupuncture groups. Demographics in both groups were statistically similar. There were no significant differences in the severity of withdrawal symptoms between the 2 groups.

An observational study on the use of auricular acupuncture in a residential treatment program was described by Martin Alster (2010). In this setting, auricular acupuncture, using the NADA model was implemented 1-3 times weekly along with mindfulness meditation. Most clients received 3-6 treatments. Non-specific benefits included feelings of contentment and relaxation. More specific improvements in symptoms included better sleep, reduced cravings

and anxiety as well as general improvement of mood. Negative reports voiced by participants were occasional feelings of lightheadedness or burning at the needle site. The staff were concerned that the treatment was time-consuming and labor-intensive. The staff also observed that the group dynamic was a factor in both the participants' willingness to participate or, in some cases, their refusal to do so.

In another qualitative study (Bergdahl et al., 2014) similar findings of increased relaxation, feelings of well-being, peacefulness and harmony, as well as decreased anxiety and drug use with auricular acupuncture were reported. Concerns voiced by the participants were that the process was time consuming, the effect was short-term, there was dependence on someone else to give the treatment, and that cravings remained after treatment termination.

Massage, Meditation and Yoga

Many other modalities involving relaxation have been used to decrease the anxiety and stress symptoms associated with substance use withdrawal. Studies generally report improvement of symptoms but difficulties identifying appropriate control groups continue to plague these studies.

A study of chair massage (N=40) over 3 days was compared to relaxation therapy (N=42) as the control condition (Black et al., 2010). Participants were recovering from alcohol, cocaine or opiate withdrawal. Anxiety was measured using the Speilberger State /Trait Anxiety Inventory (STAI). Anxiety was reduced in both groups but to a greater extent in the Chair Massage (CM) group (state, $p= 0.001$ and trait $p=0.045$). The state anxiety decrease was sustained for over 24 hours in CM, but not in the relaxation therapy control group. Standard counseling and pharmacological management were also included. Standardized procedures were used for each

group to include the same time each day, same length of time, same room, same physical lighting and the same staff member in the room. There was no physical contact with the participants. Content validity and internal consistency of STAI (r=0.83) as well as benchmark for anxiety were addressed. Heart rate response demonstrated no significant difference. An incidental finding of a mean downward trend in diastolic blood pressure was observed in both groups (p>.0001). This may have been related to a physiological response to decreased anxiety but was not addressed by the author.

Another study of massage therapy identified a reduction in anxiety and also in heart rate (Reader, Young, & Connor, 2005). This study of patients during the first four days of alcohol withdrawal identified a decrease in pulse rate of 3-4 beats per minute after 15 minutes of upper body massage. The control group was treatment as usual. However there was no comment on how long the lower pulse rate lasted. The confounder of increased attention to the participants could have affected the results (Reader et al., 2005).

Meditation has also been extensively used in substance abuse treatment. A study using qigong meditation (QM) was compared to stress management and relaxation training (Chen, Comerford, Shinnick, & Ziedonis, 2010). Chen et al. (2010) described QM as an interaction of a variety of Chinese exercises and therapies, described as integrating body, breath and mind into 'oneness'. Yoga and transcendental meditation are considered forms of QM. The process includes slow abdominal breathing, inward attention, guided imagery and focus on maintaining an 'empty mind'. Participants in both groups followed recorded instructions. This study showed no significant difference in state anxiety between the stress management and relaxation training group and the QM group. Both groups noted decreased anxiety at the end of two weeks. The

expected decrease in anxiety over time was not addressed. Individuals with low group participation had more anxiety at the end of week two than participants who regularly attended either of the two treatment groups. The participants also discussed the barriers they identified to completing the meditation program. Comments included “too much for me”, “too much on my mind”, “cannot concentrate”, “not sure how it can help”, “should not occur during free time”. Many participants would have liked to have had the yoga integrated with regular activities, not as an additional activity. There was no discussion on increased time in recovery.

Mindfulness meditation has also been studied in substance abuse recovery (Alterman, Koppenhaver, Mulholland, Ladden, & Baime, 2004). In this study, meditation did not affect the results of the Addiction Severity Index (ASI) when measured over 5 months during the patients’ stay in residential treatment for substance abuse. (N=31). With mindfulness meditation, breathing is used as the focus of attention for meditation. Emphasis is placed on paying attention to restlessness and irritability, then attempting to calm physiological responses of the body and calm the mind. In this population, extra attention was placed on managing impulsivity and its relationship to substance abuse. There was no evidence that this training had better outcomes than treatment as usual. However, the authors commented that this treatment might be more helpful in specific populations such as those with higher interest in religiosity or spirituality.

The relationship of spirituality to the effects of mindfulness and yoga was described by Khanna and Greeson (2013). Their review of complementary treatments in substance abuse found support for the use of yoga in conjunction with mindfulness in treatment. This combination of therapies appeared to enhance recovery from addictive disorders, by targeting stress-related cognitions, emotions, and drug craving. There was also evidence that when yoga

and meditation targeted individuals with high spirituality there was a significant decrease in cortisol production (31%) after each session that was not found in those who used yoga for physical exercise only (Smith, Greer, Sheets, & Watson, 2011). Yoga was often referenced as an adjunct activity available in recovery programs and also in therapy sessions for individuals still in the preparation phase of substance abuse recovery (Chen et al., 2010, Khanna & Greeson, 2013). Unfortunately, no RCTs specifically involving yoga were found related to substance abuse recovery treatment.

Ospina et al. (2008) completed a systematic review of meditation clinical trials between 1956 and 2005 including mindfulness, yoga, T'ai chi and QM. Issues with many studies included publication bias, empirical evidence varying between the quality of the study and the effect of treatment, self-selection into groups, motivation to participate as well as difficulty in blinding both the control and experimental groups. The authors felt there were threats to validity at all levels despite statistically significant improvements in many studies (Ospina et al., 2008).

Music Therapy

Music has been used as an adjunct therapy in substance abuse treatment for many years. A systematic review by Mays, Clark, and Gordon (2008) identified music as an adjunct therapy in 5 studies with participants generally feeling that music was 'helpful'. Reports were qualitative and no RCTs were available. Bonny in her seminal writing in 1986 identified music as a non-verbal therapy which activated emotions and a physiological response, produced symbolic images and enhanced the other senses. However, only 14% of substance abuse treatment programs offer music therapy (Aletraris, Paino, Edmond, Roman, & Bride, 2014). More recently

there has been renewed interest in the concept of binaural beats imbedded in music having an effect on mood. In this systematic review (Chaieb, Wilpert, Reber, & Fell, 2015) there was some evidence of decreases in both state and trait anxiety with regular sessions, however no RCTs have been published related to substance abuse recovery. The authors mentioned that further research was needed to identify neural mechanisms as well as sound ranges most likely to be effective (Chaieb et al., 2015).

Other Somatic Treatments

During the past decade there has been renewed interest in the use of modulating neurohormones through the use of electrophysiology. Manipulating behavior and cognition through the use of electrical currents has been used for over 70 years, primarily as Electroconvulsive Therapy (ECT) for the treatment of severe depression. There was some interest in the effect of ECT on substance abuse in the 1990s. However, individual positive case studies (Pearlman & Savanin, 1999) did not lead to RCTs indicating effectiveness on a broader scope (Moss, & Vaidya, 2014). More positive results have been identified using other modalities.

Deep Brain Stimulation

Deep Brain Stimulation (DBS), a neurosurgical procedure involving the placement of directed electrodes within the brain, has been developed to treat movement disorders such as Parkinson's disease and other neurological conditions associated with severe tremor. The electrical stimulus appears to interact with the corticostriatal circuits and associated neurons (also highly implicated in substance abuse) but the exact mechanism of action is unknown (Soyka &

Mutschler, 2015). Pierce & Vassoler (2013) theorized that targeting the nucleus accumbens and sub thalamic nucleus may hold promise for an effect on substance abuse. Although individual reports and case studies have been reported in which an effect on substance abuse was found, completing an RCT has proven difficult as patients are reluctant to enroll for this invasive procedure (Luigjes, Brink, Schuurman, Kuhn, & Denys, 2015). More research studies are available using non-invasive technologies.

Transcranial Magnetic Stimulation

About 20 years ago Trans-cranial Magnetic (TMS) therapy was introduced and studied for the treatment of depression and other neurocognitive disorders. It is presently FDA approved for use in resistant depression. Repetitive (r) TMS is based on the theory that a magnetic field passing through the cranium, induces an electrical field that can alter neuronal activity. The primary target for rTMS in the treatment of substance uses disorders is the dorsolateral prefrontal cortex (DLPFC) (Gorelick, Zangen, & George, 2014). The DLPFC assists in the regulation of the limbic system through its involvement in higher-order executive functions such as self-control and being aware of behaviors and related events which are intimately involved in substance abuse (Goldstein & Volkow, 2011). Interest in rTMS in substance abuse occurred after the publication of case studies of patients exposed to this therapy for depression who noted improvement in their craving symptoms. This has led to further research studies.

Jansen et al. (2013), in a meta- analysis, reviewed 9 sham controlled studies involving substance abuse. Three studies involved alcohol use and identified an effect on craving reduction ($p = .06$). There were no differences in craving reduction across other substances: nicotine, and food. These studies involved active substance abuse rather than individuals in

recovery. In another literature review, Grall-Bronnec, and Sauvaget (2014), identified 18 studies using rTMS to treat substance abuse. Eleven studies supported the efficacy of rTMS in the reduction in craving which was usually measured using a visual analog scale (VAS). However, these effects were short-term which was thought to limit the effectiveness of the treatment. A small RCT identified a decrease in alcohol craving in a single blind, sham controlled study of 45 patients with alcohol dependence (Mishra, Nizamie, Das, & Praharaj, 2010). Thirty patients were in the active group. High-frequency rTMS to the right DLPFC was used for a total of 10 sessions. Alcohol craving, using the Alcohol Craving Questionnaire (ACQ-NOW) was measured at base line, after the last rTMS session and 1 month later. Effect size for treatment with time was moderate ($r = 0.401$). Decrease in craving at 30 days was significant ($p<0.0005$). This study was criticized due to concerns regarding placebo effect, the use of rTMS only on the right DLPFC as well as limiting measurement to subjective identification of craving (Trafton, 2010).

A subsequent study was conducted by Mishra, Praharaj, Katshu, Sarkar, and Nizamie, (2015) in an attempt to decrease this criticism. This study was double blinded using 20 patients with alcohol dependence syndrome randomly assigned to receive rTMS over either the right or left DLPFC, using the same settings as in the previous study. Measurement was the ACQ-NOW at the same time points. The results showed no difference between groups and time but did identify significant reduction in craving scores in both groups over time ($p < 0.0001$).

Use of rTMS in substance abuse recovery shows promise. However the limitations with the present studies include no references to, or identification of, long term recovery or use of repeated treatments over extended periods. Transcranial magnetic stimulation appears to be a

safe modality based on use for psychiatric disorders but more research is needed before moving this modality into substance abuse treatment.

Transcranial Direct Current Stimulation

Transcranial direct current stimulation (tDCS) is a recent addition to the electrophysiological tool box of substance abuse treatment modalities. This method (tDCS) was initially researched in the 1960's; however no significant results were published. Little research was reported until the past decade when results of research involving rTMS stimulated renewed interest in tDCS. Direct current stimulation is applied using a simple devise, obtainable on the internet and charged with a 9 volt battery. This devise provides a very low direct current (1-2 mA) in a single direction from the anode to the cathode attached to the cranium with saline moistened sponges and a strap (Rosa, & Lisanby, 2012). The focus of current research is also on applying the current to the DLPFC and the subsequent effect on cognition, mood and behavior. Few research studies using tDCS relating to substance abuse and craving are available.

Jansen et al (2013), in a meta-analysis of 8 studies of tDCS compared results of rTMS to tDCS, and found comparable decreases in alcohol craving ($z = 5.832$, $p < 0.001$). These devices are not FDA approved for any specific disorder, however, they are available without a prescription from multiple internet sources. They are advertised as providing low level electrical current to the brain for various neurocognitive problems.

Cranial Electrotherapy Stimulation (CES)

Cranial Electrotherapy Stimulation was developed in the Soviet Union in the 1950s and has been used in the United States since the 1960s, initially as a treatment method called 'electro sleep'. Low level (100 to 600 microamps) micro current is given to the patient through electrodes placed on the earlobes for a varying amount of time (Kirsh & Smith, 2000). The device is presently used in the Veterans Administration System (Tan, Dao, Smith, Robinson, & Jensen, 2010) and by psychologists in general practice for the ancillary treatment of pain, anxiety, depression and insomnia, (Kirsh, & Gilula, 2007). Research protocols in a variety of patient conditions have varied from a single treatment, a one hour treatment weekly to 20-30 minute sessions daily over several weeks. Initial CES studies focused on anxiety in a substance abusing population were conducted 20 years ago (Schmitt, Capo & Boyd, 1986; Overcash & Siebenthall, 1989; Krupitsky et al.,1991). Results in all these studies were described as statistically significant, although only Krupitsky et al. (1991) identified a p value ($p<.05$). No negative side effects were identified. However, no recent studies have been conducted to evaluate relief of anxiety in substance abuse withdrawal.

The use of CES in Generalized Anxiety Disorder has also been studied (Bystritsky, Kerwin, & Feusner, 2008). In a small open label study ($N = 12$), participants ranging in age from 29-58 years were recruited from the community. All received an active CES unit. There was no control group. CES was administered for 6 weeks using a 0.5-Hz frequency and a 300-u1 A intensity. Both the Hamilton rating Scale for Anxiety (HAM-A) and the Clinical Global Impressions-Improvement scale (CGI-I) were used to measure anxiety pre- and post-treatment. Fifty percent (6 patients) had a 50% decrease in the HAM-A ($p = .01$) and a rating of 1 or 2 on the CGI-I (much improved, or very much improved). An additional patient had significant

improvement in anxiety score but did not meet criteria for the study standard. Adverse events mentioned were mild headache or nausea. A limitation of the study mentioned by the authors was the small sample size and that it was open label, which may have impacted on the results.

A similar study by Barclay and Barclay (2014) evaluated CES in a group of primary care patients (n=115) with anxiety disorders. In this double blinded study, participants were recruited from the community and paid $30 to enroll in the 5 week study. Individuals in the placebo group were given an opportunity to use the active unit following their completion in the study. In this study, 85% of the participants in the active CES group had an overall reduction in anxiety at study termination. The average reduction was 32% from anxiety baseline as measured with the HAM-A (F=43.401, df =1 p=.001, d=.94).

Other researchers have also reported positive study results using CES. A double blinded study using CES to decrease anxiety during dental procedures is often referenced (Winick,1999). In this study (N=33), 17 patients were randomized to the experimental group using CES at 0.5 Hz and a sub sensory A setting of 200-u1, while the 16 patients in the placebo group had sham CES units. The manufacturer did not release the codes for active or placebo units until after the study was completed. Measurement was a 7 point Likert scale which rated the degree of improvement of anxiety at completion of the procedure and a Visual Analog Scale (VAS) measuring anxiety from ‘not anxious’ to ‘very anxious’. The measurements were taken at 3 time points during the procedure: prior to initiation, midway, and at completion. Both the dentist and the patient completed both ratings at each time period. (The dentist rated his perception of the patient’s anxiety). Results of the VAS for both patient and dentist observer indicated decreased

anxiety in experimental group when compared to the placebo group ($p < .02$) and this was corroborated with the Likert results ($p < .01$) (Winick,1999).

Another double blind study examined the effect of CES on sleep and depressive symptoms in 42 care givers of patients with Alzheimer's disease. This study found no statistically significant differences between the placebo and experimental groups (Rose, Taylor, & Bourguignon, 2009), although there was trending towards significance on the sleep index. The authors felt that a limitation was that the study was underpowered.

Empirically, CES appears to assist in bringing neurotransmitters back into homeostasis. However, the exact mechanism of action remains unclear. This effect is thought to be due to the effect on the parasympathetic nervous system through stimulation of the auricular branch of the vagus nerve (Kirsh & Gilula, 2007). By changing the electrical and chemical activity in the brainstem, CES appears to amplify activity in some neurological systems and diminish activity in others. Critique of many studies included low power due to few participants, methodological differences and difficulty controlling for multiple variables (Bystritsky et al., 2008; Rose et al., 2009). Although CES has been studied in patients with various anxiety related disorders, and appears to be effective, no recent studies have focused on anxiety in the period of early substance abuse recovery.

Summary

The heterogeneity of substance abuse and its effect on individuals is a conundrum for researchers. The thread throughout these presented studies is that RCTs are difficult to conduct due to the multiple variables associated with individuals in recovery for substance abuse. Demographics may be similar, as may be the substance of abuse, but each individual comes with

his or her own genetic makeup and unique epigenetic changes. Although RCTs remain the gold standard for research, they are challenging to complete or reproduce in substance abuse treatment due to multiple variables associated with small treatment populations in individual recovery programs. This heterogeneity of substance use disorders with the widely differing individual responses to treatment portend a need for individually developed treatment plans. As research moves into practice, it is critical that all potential modalities which may enhance epigenetic reversal, and improve the sustainability of substance abuse recovery be assessed for use in each individual. Most but not all of these complementary modalities have been found to decrease either anxiety or craving in specific individuals with substance use disorders. Cranial electrotherapy stimulation is a modality that seems especially promising since it does not require individual monitoring or specialized group attendance, and if effective may be used by individuals on an ongoing basis. The effect of CES on decreasing anxiety in non-substance abusing populations appears to be robust. This effect may also be apparent in substance abusing populations. However previous studies in early substance abuse recovery are limited and have not been replicated in many years. Research in all these modalities should be continued, and when found effective, be implemented into practice for developing individual integrated care models needed for enhancing and sustaining recovery in each substance abuser.

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CHAPTER 3: THE EFFECT OF CRANIAL ELECTROTHERAPY STIMULATION AS A METHOD TO DECREASE ANXIETY SYMPTOMS FOLLOWING OPIATE AND ALCOHOL WITHDRAWAL

Abstract

Background: Almost 35% of men suffering from alcohol or opiate dependence drop out prior to completing residential programs of 30 days or less. Anxiety is often a quoted reason for early dropout. Supplemental interventions designed to promote tenure in residential treatment are sorely needed for men who are substance abusers.

Purpose: The purpose of this study was to determine if Cranial Electrotherapy Stimulation (CES), which is FDA approved for the treatment of anxiety and depression, would decrease anxiety in substance abusing men in early recovery.

Methods: A double blind experimental study using repeated measures and two treatment conditions (intervention/active and control/placebo) was conducted over a period of 15 days during the first 3 weeks of opiate/alcohol abstinence. Salivary Cortisol and state anxiety were measured on the first and final day of CES treatment. Anxiety was also measured on all participants at study enrollment and at 30 days.

Results: Fifty nine participants completed the study. Anxiety and cortisol responses improved in both groups. While differences were not significant, the cortisol decrease was greater in the active treatment group than in the placebo group. In addition there appeared to be a trending downward in momentary anxiety as measured in the active group.

Conclusions: CES may be effective in reducing anxiety and cortisol response in this population; however it was not demonstrated statistically in this study. Psychopharmacological medications as well as placebo effect may have confounded the results. More research is needed in this area.

Introduction

Substance abuse is an individual and public health problem that costs the United States more than $0.5 trillion annually in health care, lost earnings, and associated crime or accidents (National Institute of Drug Abuse [NIDA], 2012). A majority of substance abusers are men. Indeed, over one quarter of the 8.5 million men arrested in 2010, were arrested for charges relating directly to substance abuse (Bureau of Justice Statistics, 2012). Approximately 1 million people access residential substance use treatment each year. Of these, two-thirds are men, many of whom are referred directly from the Criminal Justice system (Substance Abuse and Mental Health Services Administration [SAMHSA], 2012).

Men are more likely to abuse opiates and alcohol than women (SAMHSA, 2012) and they also start substance abuse at a younger age than women. However, they enter treatment later, making them at greater risk for poorer treatment outcomes, having less family support and greater involvement with criminal activity (Grella & Joshi, 1999). Almost 35% drop out prior to completing residential programs of 30 days or less (SAMHSA Office of Applied Studies, 2009). Hence, supplemental interventions designed to promote tenure in residential treatment are sorely needed for men who are substance abusers. The purpose of this study was to investigate whether Cranial Electrotherapy Stimulation (CES) would decrease anxiety symptoms and increase retention in treatment.

Background

Anxiety is the most common and disabling of the acute withdrawal symptoms (McGuinness & Fogger, 2006) and has been identified as a significant reason for treatment dropout and subsequent relapse (Levy, 2008). Anxiety generally peaks within two weeks of

substance abstinence (Ganzel, Morris & Wethington, 2010; Sher, 2002), but may persist for many months. Anxiety also affects individuals' ability to learn and complete the cognitive tasks needed to successfully complete residential treatment (Burriss, Ayers, Ginsberg, & Powell, 2008).

Anxiety symptoms are a product of continued sympathetic stimulation (Koob, 2005). In the substance abuser, this occurs when the hypothalamic-pituitary-adrenal (HPA) axis is stimulated by the neurohormones which are dysregulated during withdrawal of the substance of abuse (Lovallo, 2006). Various medications are presently used to attenuate the anxiety symptoms associated with this dysregulation in an effort to enhance program participation and continuation in treatment. The most effective medications for relief of anxiety are the benzodiazepines. However, medications in this class are not appropriate for use in a substance abusing population as these medications, which have a high addictive potential, may create further addictive behavior in these individuals (Casher, Gih, & Bess, 2011).

Other pharmaceutical agents approved for anxiety relief such as buspirone, hydroxyzine, trazodone and doxepin have limited efficacy (Casher, Gih & Bess, 2011). In addition the antihistamine and anticholinergic side effects of dry mouth and sleepiness may make them less tolerable. Many other medications administered to treat anxiety are used "off label" and include atypical antipsychotic and antiepileptic drugs (McGuinness & Fogger, 2006; Pollack et al., 2008). Antipsychotic and antiepileptic medications decrease negative emotions, and also attenuate cognitive processing and produce daytime sedation (Gilula & Kirsch, 2005). These unwelcome side effects limit the cognitive resources available for developing anxiety management skills.

Providing recovering addicts with anxiety management skills during the early post-acute withdrawal period is critical to sustaining recovery (Gil-Rivas, Prause,& Grella, 2009; Gossop, Stewart, Browne, & Marsden, 2002). As substance-abuse treatment for men focuses on group therapy and psychoeducation, participants need to be able to concentrate in order to participate fully in treatment offered to acquire these skills. This underscores the need for new, non-pharmacological approaches to manage anxiety during the acute withdrawal period that occurs early in the recovery process.

Cranial electrotherapy stimulation (CES) is a non-pharmacological approach to anxiety management that may have promise to improve retention in residential treatment and decrease early relapse. CES was developed in the Soviet Union in the 1950s, and first used in the United States in the 1960s to treat insomnia via a method then referred to as electro sleep (Kirsh & Smith, 2000). The technique was later approved by the U.S. Food and Drug Administration (FDA) (2011) for use in the treatment of anxiety as well as depression and sleep disorders. CES is presently used in the Veterans Administration System (Tan, Dao, Smith, Robinson, & Jensen, 2010), as well as in general practice for adjunctive treatment of anxiety, depression, and insomnia.

It (CES) is believed to reduce anxiety symptoms through pulsed alpha wave alternating current which affects neurotransmitters in the limbic system and subsequent downstream engagement of the parasympathetic nervous system (Giordano, 2006; Gunther & Phillips, 2010). This alpha wave stimulation ultimately results in decreased (more normalized) cortisol production (Bystritsky, Kerwin, & Feusner, 2008; Kirsh & Gilula, 2007).

The beneficial effect of alpha wave stimulation on cortisol regulation may be particularly promising for individuals in substance abuse treatment as sustained elevations of cortisol are known to occur during this time (Li et al. 2008; Lovallo, Dickensheets, Myers, Thomas, & Nixon, 2000; Sinha et al. 2011). A blunted cortisol response (cortisol levels not quickly returning to pre-stress baseline) to short stressful situations has also been identified in alcoholics and polysubstance abusers (Daughters, Lejuez, Kahler, Strong, & Brown, 2005; Lovallo et al., 2000). In addition, Daughters et al. (2005) noted that substance abusers were more likely to drop out of residential treatment if cortisol did not return to the expected baseline after completing a stressful task.

To date, no studies have addressed whether a more normalized (less blunted) cortisol response occurs in early recovery when an individual is treated with a single episode of CES. Nor have studies addressed whether a CES related change in the cortisol response is associated with a momentary reduction in anxiety (i.e: state anxiety), or whether repeated use is associated with a reduction in anxiety lasting a few days.

A Meta-analysis of 15 CES treatment studies (n=335) published by Kirsh and Gilula, (2007) provides evidence of a therapeutic effect in decreasing anxiety and other somatic symptoms (r = .65+8) among a variety of substance-abusing populations being treated in various settings. CES treatment was found to be effective for relieving anxiety in a non-substance abusing population with hour long treatments over several weeks (Bystritsky, Kerwin, & Feusner, 2008, Barclay & Barclay, 2014). A positive effect was also identified during a single treatment for state anxiety exacerbated by dental procedures (Winick, 2009). This suggests that (1) a single treatment of one hour may decrease cortisol level as well as state anxiety, and (2)

multiple treatments over several weeks may be effective in decreasing anxiety in substance abusers during the time in residential treatment.

Purpose

The purpose of this study was to determine if Cranial Electrotherapy Stimulation (CES), which is FDA approved for the treatment of anxiety, depression and insomnia, would decrease anxiety in substance abusing men in early recovery. Decreased anxiety in residential treatment has been identified as a factor associated with remaining in residential treatment (Hutchison, 2016. Chapter 4).

Method

Design

A double blind experimental study using repeated measures and two treatment conditions (intervention/active and control/placebo) was conducted over a period of 15 days during the first 3 weeks of opiate/alcohol abstinence. Anxiety and PTSD symptoms were measured at study enrollment. Anxiety and depression symptoms were measured at 30 days (study completion).

Study AIMS

- AIM 1: to compare in men in early substance recovery treatment for substance abuse the effects of Cranial Electrotherapy Stimulation or placebo on anxiety and depression.
- AIM 2: to compare in men in early substance recovery treatment for substance abuse the effects of Cranial Electrotherapy Stimulation or placebo on cortisol level.

Setting and Sample

The setting for this study was a Level II residential treatment program for men which is operated by the Center for Drug Free Living (CFDFL) and certified by the Commission on Accreditation of Rehabilitation Facilities. Only the Level II program clients residing on campus were eligible for study enrollment. A level II program was selected as this provides up to 6 hours of psychosocial support daily in a structured environment. The treatment program includes daily group sessions with psychoeducation, as well as weekly individual counseling. In this environment, participants could be monitored for compliance with the treatment protocol.

Participants were initially recruited during their stay in the medical detox facility when the PI discussed the study during the weekly community meeting. All clients completing an alcohol or opiate medical detox were eligible to participate if they met the administrative criteria for admission into the Level II residential treatment program and intended to stay in treatment for at least 30 days. Individuals with mental health disorders were not excluded if they were considered appropriate for residential treatment. Exclusion criteria were: (1) having an implantable electrical device (this exclusion criterion was recommended by the CES manufacturer); (2) unable to read or understand English; (3) recent dental surgery or bleeding oral lesions (blood in the salivary cortisol specimen affects accuracy of measurement). Four to six individuals who met the study criteria were typically admitted every week. Approximately five months were required to enroll 79 study participants.

Study Measures

A demographic questionnaire was used to assess age, education, race/ethnicity, housing situation prior to admission, primary substance of abuse and mental health disorders prior to

admission. Additional variables included chronic medications and previous residential treatment admissions. Symptoms of PTSD and depression were also collected as independent variables.

The PTSD Checklist—Civilian Version (PCL-C) was used to assess for symptoms of posttraumatic stress disorder (PTSD) which clients were presently experiencing Mental Illness (Research, Education and Clinical Centers [MIRECC]. n.d.). This self-administered instrument has been in general use for more than 20 years in both military and civilian populations (Orsillo, 2001). Scores of less than 29 are considered not significant for PTSD, while those above 45 are considered of high enough severity for continuing with the assessment for the diagnosis of PTSD. The PCL consists of 17 items identified with the diagnosis of PTSD in the DSM, and uses a 5 point Likert scale. Internal consistency is high (r = .75) across studies in various populations (Wilkins, Lang, & Norman, 2011).

Anxiety experienced since leaving the detox facility was measured using the Zung SAS (Zung, 1971). This self-administered anxiety scale is used for identifying anxiety symptoms that have occurred within the past few days. The Zung is a 20 item measure of somatic and psychological symptoms reflecting on feelings over the identified time frame. Each item is scored using a 4 point Likert scale with 5 items being reverse scored. Anxiety scores between 45 and 60 are considered moderate anxiety, and scores between 60 and 74 are considered severe anxiety. A raw score of > 36 is clinically significant for difficulty carrying out normal work or activities (Zung, 1980). The Zung has good reliability (r = .71, alpha = .798; Zung, 1971) and content validity when compared to the Hamilton Anxiety scale (r =.75) (Sharpley & Christie, 2007). The Zung scale has been used in various populations for research and clinical assessment since its development in 1971 (Sharpley & Christie, 2007).

Depression was measured at 30 days in recovery treatment using the Patient Health Questionnaire (PHQ-9). This depression scale was originally developed by Spitzer, Williams, and Kroenke (1999) with a grant from Pfizer Inc. The PHQ-9 is a 9-item self-report measure that assesses the nine depression symptoms from the DSM-IV depression criteria (Kroenke et al., 2001). Each item is scored on a 4-point scale (0–3) and scores range from 0 to 27. Similar to the Beck Depression Inventory (BDI), the summed scores can be used to describe the patient's symptoms in one of five interpretive categories: none (0–4), mild (5–9), moderate (10–14), moderately severe (15–19), and severe (20–27). A cut-off score of > 10 is generally used to identify individuals likely to have major depressive disorders (Kroenke, et al., 2001). The PHQ-9 has been shown to be highly correlated (r =0.76) with the Beck Depression Inventory and has good internal consistency (r =.87) when used in residential substance abuse treatment (Hepner, Hunter, Edelen, Zhou & Watkins, 2009).

State anxiety was measured using the 6 item State-Trait Anxiety Inventory (STAI-6; Marteau & Bekker, 1992). The STAI-6 is a self-administered measure of state anxiety. This 6-item version of the Speilberger STAI (Tiuczek, Henriques, & Brown, 2009) correlates well with the full (20 item state anxiety) STAI (r=.95) and has good internal consistency (alpha = .82) as well as excellent construct validity in clinical populations (Court, Greenland, & Margrain, 2010).

Cortisol was collected using a commercially prepared self-collection kit designed to measure salivary cortisol and was provided by Salimetrics (Salmetrics 2011), the laboratory chosen to evaluate the cortisol levels. This laboratory provided support for collection and shipment, in addition to performing salivary cortisol assays (Salimetrics, 2012). The average morning cortisol level reported by Salmetrics (2012) for adult males between ages 31 and 50 is

0.122 - 1.551. Salimetrics uses a duplicate sample of saliva and a highly sensitive immunoassay which has a lower limit of sensitivity of 0.003ug/dl and a standard curve ranging from 0.012ug/dl to 3.0 ug/dl. The average intra-assay coefficient has a variation of 3.5% and inter-assay coefficient of variation of 5%. Serum and saliva samples show strong linear relationship ($r = .91$, $p < 0.0001$) which is consistent with McCracken & Poland's (1989) work indicating a strong connection between salivary and circulating cortisol ($r = .78$, $p < .03$) when both are measured over time within the same individual.

Procedure

Each participant had a uniquely numbered CES unit assigned to him on day 1 of the treatment period. The unit was randomly pulled from the box of units by the PI when directions for use were being reviewed prior to the first treatment. This unit was then labeled with his name. Neither the participant nor the PI was aware of whether the unit was a placebo or active CES unit. The participant picked up his unit each day, applied saline solution to the ear clips and attached them to his ear lobes. He then turned on the unit as instructed and proceeded with normal activities until he returned it to the storage bin an hour later when the unit automatically turned off. At that time he signed the log book to validate time and length of use. The log book was checked daily by the PI or the facility nurse to insure compliance with instructions.

The three week CES treatment period began during the first week following the medical detox and continued for a total of 15 daily one hour sessions over the following three weeks. If participants were unable to complete the number of treatments within this time frame they were withdrawn from the study.

Data Collection Procedures

Salivary Cortisol was collected on the first and final day of CES treatment, before and after the daily CES treatment session scheduled for that day for all participants. Cortisol was measured between 0815 and 0845 am and again between 0930 and 1000 am following completion of the hour long treatment on these days. As morning cortisol levels usually peak within 2 hours of arising and then gradually decrease during the day, collection at these time points allowed for consistency between participants. State anxiety, using the STAI 6 was collected at these same 4 time points.

Anxiety symptoms experienced during the past few days were measured using the Zung SAS on all participants at study enrollment and at 30 days. PTSD symptoms, using the PCL-C, were measured on admission. Depression, using the PHQ-9, was measured at 30 days as recommended in the literature (Hepner et al. 2009).

Each participant received a gift card to a big-box retail store (Walmart) at two time points: Completion of the second salivary cortisol and STAI-6 on the day one (first) treatment session ($5), and after completion of the Zung SAS, and the PHQ-9 on day 30 of residential treatment ($10).

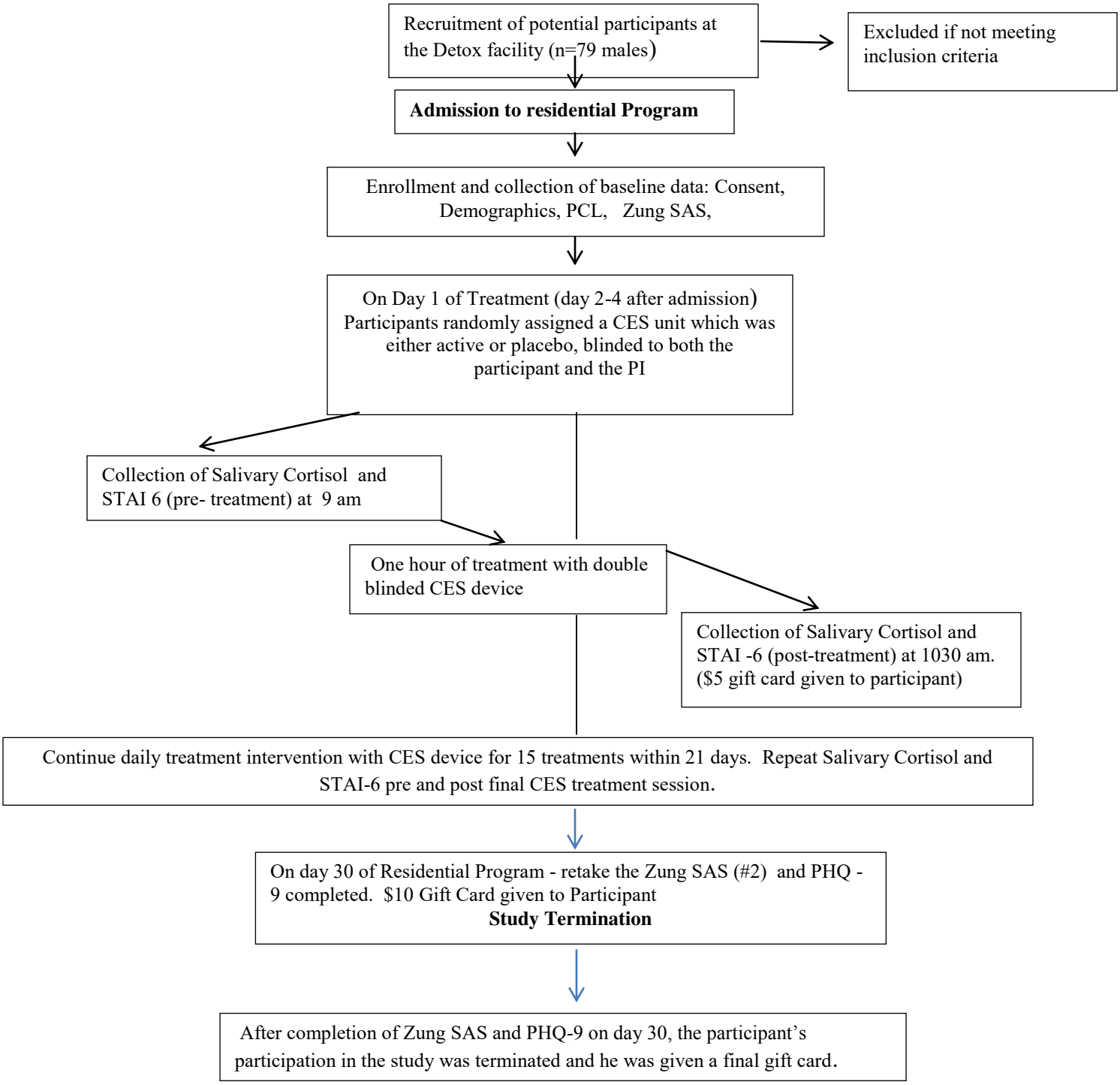

Figure 1: Flow of Participants through the study

Data Analysis

Descriptive statistics (e.g., mean, standard deviation, frequency, and percentage) were calculated for all demographic variables to summarize sample characteristics and properties of the key study variables, including the proportion of participants with and without PTSD and/or depression in each study condition. Differences in the demographic characteristics of the placebo and experimental group were investigated with Chi-square analysis for categorical data and t tests for continuous variables. An alpha level of 0.05 was used in these analyses and in those used to address study hypotheses and research questions.

Ethical Considerations

This study was approved through the University of Central Florida Institutional Review Board. Participation in the study was voluntary and not a requisite for enrolling in residential treatment. There were no significant adverse effects identified during the use of this CES device during this study.

Results

A convenience sample of 79 adult male participants who met study criteria were recruited for the study between October 2013 and April 2014. Approximately 110 individuals were admitted into the residential treatment program for treatment of alcohol or opiate dependence following inpatient detox during the study period; 81 volunteered for entry into the study. Two individuals were subsequently withdrawn by the investigator due to severe medical problems during the first few days in treatment. The remaining 79 were randomized into either the control/placebo or experimental group.

Of the 79 randomized participants, 19 subsequently dropped out of the study. One participant asked to be withdrawn and eventually finished residential treatment. One participant was withdrawn by the PI as he was unable to complete all requirements within the study time constraints, and eventually dropped out of treatment. The remaining 17 participants either left the program, or were terminated by the administration due to drug use (relapse) in the facility. Sixty participants completed the required number of CES treatments and 57 completed the 30 day post treatment psychological inventories. The attrition rate was approximately 24%, resulting in a sample for analysis of 57. Assuming a power of .80 and an alpha of .05, a sample of 56 was estimated to be sufficient to detect a moderate (0.25) effect.

Sample Characteristics

There were no significant differences on the pretreatment demographic variables between the active and the placebo group of study completers. Table 1 provides demographic data by treatment group. The average age in the intervention group was 39 and 41 for the placebo group. The majority of participants in both groups were European/White race, homeless, educated at the high school level or higher and their primary substance of abuse were opiates.

Table 2: Population demographics of study completers

Variable	Intervention n=29	Placebo n=31	p value for X^2	Total n=60
	n(%)	n(%)		n(%)
Age groups			p =.40	
Less than 30	6 (10%)	10 (16.6%)		16 (26.6%)
31-50	15 (25%)	13 (21.6%)		28 (46.6%)
Over 50	8 (13.3%)	8 (13.3%)		16 (26.6%)
Race/Ethnicity			p =.80	
European/White	21 (35%)	20 (33.3%)		41 (68.3%)
Hispanic	5(8.3%)	8 (13.3%)		13 (21.6%)
African American	3 (5.0%)	3 (5.0%)		6 (10.6%)
Living situation prior to treatment			p=.15	
Family or self	6(10.0%)	6(10.0%)		12 (20%)
Living with parents	0 (0.0 %)	5 (8.3%)		5 (8.3%)
Transitional housing or friends	5(8.3%)	6 (10.0%)		11 (18.3%)
Homeless	18 (30.0%)	14 (23.3%)		32 (53.3%)
Years of Education			p=.62	
< High School	4(6.6%)	7 (11.6%)		11 (18.3%)
GED	9 (15.0%)	6 (10.0%)		15 (25.0%)
HS Diploma	7 (11.6%)	9 (15.0%)		16 (26.6%)
college/trade/AA	9(15.0%)	9 (15.0%)		18 (30.0%)
Primary Substances of Abuse			p=.98	
Opiate	12 (20.0%)	12 (20%)		24 (40%)
Alcohol	9 (15.0%)	10 (16.6%)		19 (31.6%)
Poly substance with opiate	8 (13.3%)	9 (15%)		17 (28.3%)

The mean age of the dropout group was 35 compared to 41 in the completers. All of the participants in the drop out group were opiate dependent while 32% of the study completers had a primary diagnosis of alcohol dependence. Opiate users are known to drop out earlier than alcohol users as their symptoms are often more severe and protracted. Of interest is that completers endorsed more PTSD symptoms but less anxiety symptoms on admission and there was a difference between the STAI 1 and STAI 2 in these groups. The other demographic markers of the participants were similar to that of the general population of clients admitted to this program. Eleven of the 19 dropouts were in the active CES group.

Primary Outcome Measures.

The effect of CES treatment on generalized anxiety (Zung SAS), on state anxiety (STAI-6), as well as on Depression (PHQ-9) was analyzed. There were 31 participants in the placebo group and 29 in the experimental (active CES) group.

The participants had mean baseline Zung SAS scores of 43.55 (10.65) in the placebo group and 44.66(11.21) in the active CES group. The Zung SAS at 30 days was 35.71 (10.6) in the placebo group and 36.90 (10.38) in the CES group. Depression based on the PHQ-9 at 30 days (Study termination) was 8.46(6.06) in the placebo group and 8.31(6.02) in the active CES group. The number of participants on antidepressants at day 30 in the placebo group was 10 and 15 in the active group. Twelve of these participants were on antidepressants prior to starting treatment. There were no significant differences between groups (see Table 2).

Table 3: Effect of CES on Anxiety and Depression

Variable	Placebo CES Mean and SD	Active CES Mean and SD	P value for X^2
Zung SAS (Anxiety) on Admission	43.58 (10.65)	44.66 (11.12)	.19
Zung SAS (anxiety) at 30 days	35.71 (10.60)	36.90 (10.38)	.63
Depression (PHQ-) at 30 days	8.46 (6.06)	8.31 (6.02)	.12
On antidepressants at 30 days	10	15	.15
STAI 6 prior to 1st CES treatment	12.94 (3.97)	13.90 (4.40)	.47
STAI 6 after 1st CES treatment	11.73 (3.95)	13.01 (4.12)	.67
STAI 6 prior to last CES treatment	11.51 (4.26)	11.10 (4.08)	.73
STAI 6 after last CES treatment	11.38 (3.56	10.38 (3.56)	.44

The STAI-6 at baseline (prior to any CES treatment) was 12.94(3.97) in the placebo group and 13.90(4.40) in the active CES group. Following the first CES treatment, the results were 11.73(3.95) in the placebo group and 13.10(4.12) in the active group respectively. On the final day of CES treatment, the placebo group scored 11.51(4.26) and the active CES group scored 11.10(4.08) prior to the treatment session. Following this final session the scores were 11.38(4.51) and 10.38(3.56). While these differences were not statistically significant at any time point, greater improvement was seen in the experimental group compared to the placebo group.

Secondary Outcome Measures.

The effect of time and treatment on salivary cortisol levels was measured. Cortisol was measured between 0815 and 0845 prior to CES treatment on the first and last day of CES use (both placebo and active CES group) and again between 0930 and 1000, following completion of the hour long treatment on these days. Mean (SD) baseline salivary cortisol in the placebo group was .588 (.415) and decreased to .571 (.962) following the first treatment session. In the active group the mean (SD) cortisol level was .386 (.287) prior to treatment, and decreased to .302 (.254) following the initial session. On the final day of CES treatment, the placebo group measured .328 (.208) prior to treatment and .201(.129) following the session. The active CES group measured .340 (.193) and decreased to .168(.926) following the session (see Table 3). While these differences were not statistically significant, some interesting trends were noted. Salivary cortisol decreased in all of the participants following the initial session and continued to decrease until the completion of the program. Importantly, while not statistically significant, the active CES group showed a greater downward trend in cortisol levels.

Table 4: Effect of CES on Salivary Cortisol

Cortisol collection time	Placebo Mean and SD	Intervention Mean and SD	P value of X^2
Cortisol before 1st CES treatment	.588 (.415)	.386 (287)	.40
Cortisol after 1st CES treatment	.571 (.962)	.302 (.254	.40
Cortisol before last CES treatment	.328 (.208)	.340 (.193)	.46
Cortisol after last CES treatment	.201 (.129)	.168 (.926)	.51

Discussion

While this double blinded study identified no statistically significant differences in the response to anxiety between the experimental (CES) group and the placebo group at study conclusion, some important trends were noted. The cortisol decrease was greater in the active treatment group than in the placebo group. In addition there appeared to be a trending downward in momentary anxiety as measured by the STAI 6 in the active group at the end of the treatment phase. These differences might have been more evident in a larger study group and/or in a group focused on a single chemical of abuse: either alcohol or opiate.

The opiate dependent participants were generally younger and appeared to be less able to complete treatment as this was the only group who dropped out of the study. However, there may be other, unidentified factors affecting the results. All participants who completed the study were enthusiastic about participation and needed few reminders to come in and use the devices each day.

Since participants did not know if they were receiving the CES or the placebo, many thought they were in the experimental group and felt less anxious. There was also positive reinforcement within the study as each participant received increased social support due to multiple daily short interactions with the PI, her assistant or the facility nurse which could have influenced the outcomes. If multiple arms had been used in this study such as a treatment, placebo and control group the results might have been statistically significant. However, participants might have been more difficult to recruit into a control group (treatment as usual) if there was a perceived benefit to those in the active or placebo arms. Also, the effect of increased social support from providers or the study team may have been a factor on the decrease in anxiety in both groups over the 30 day period. The change in anxiety as manifested on the Zung

SAS was similar to that of a previous study in this population (Hutchison, 2016). Also of interest, at 30 days in the program, neither group endorsed greater than mild depressive symptoms (PhQ-9 was less than 10). However almost half the participants were on antidepressants: more participants in the active treatment group were on antidepressants when compared to the placebo group. The difference between groups was not significant as any of these participants were already on antidepressants when initially enrolled in the study. Different results may have been obtained if none of the participants were on psychopharmacological medications.

Implications

The demographic differences between the dropouts and program completers are significant in that only opiate users dropped out and were a few years younger (35 vs. 41) than those competing the study. Opiate, alcohol and opiate/alcohol combined users behave differently and perhaps should be studied separately. It may be important to recognize these differences, not only in research but also in treatment programs as the cultural and social differences in these populations may affect outcomes.

Although the use of CES in this study did not show significant differences between the two groups in this study, the participants were engaged in an activity that they perceived to be of benefit. More research is needed in this area. In addition, using CES as an option for treatment in specific individuals who identify high anxiety symptoms on program arrival may affect their treatment outcome. Individuals who have a preexisting diagnosis of generalized anxiety may also benefit from prolonged use. There was considerable variation was noted between individual responses in this study. An open label study might identify these individuals and their associated

individual characteristics. More research is needed to identify these characteristics and relationship to CES use.

Study Strengths and Limitations

This was a small double blinded study at a single treatment program and study inclusion criteria were very broad. However, because the participants were randomized to either intervention or control groups, the variability between and within groups should have been minimized. An additional confounder was that the participants were treated with pharmaceuticals for anxiety, sleep and depression when indicated and this may have affected individual cortisol and CES response.

Conclusion

Although CES has been used for many years in the treatment of anxiety, in this study, the effect of CES was not significantly greater than that of the placebo in this population. However, more research is needed in this area as the results may have been mitigated by the large number of variables. Also, there was trending towards improvement of symptoms. In future research, narrowing the criteria for study admission might decrease the number of variables. Limiting the study to participants with a single substance of abuse and a high anxiety level on admission could provide a narrower focus on anxiety outcome. An additional study measuring cortisol in a control group of substance abusing men awaiting residential placement and within a treatment as usual group of men in the residential recovery program, measured at the same time points as done in this study would be helpful. This would determine if the gradual decrease in cortisol levels noted over time was an effect of the treatment/placebo or a normal effect of time in

substance abuse recovery or another unknown factor. A slow normalizing of cortisol response is expected. Finally, in a future study, multiple arms in a trial, such as treatment, placebo and control group, might result in statistically significant outcomes.

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CHAPTER 4: TRANSLATIONAL RESEARCH APPROACH FOR NURSE CLINICIANS EFFECT OF ANXIETY ON SUBSTANCE ABUSE TREATMENT AND EARLY RELAPSE IN RESIDENTIAL SUBSTANCE ABUSE TREATMENT

Abstract

Anxiety is a recognized, co-occurring disorder associated with substance abuse, and is a prominent negative emotion experienced by many patients during post-acute withdrawal from opiates and alcohol. Although anxiety as a factor in relapse has been measured in longitudinal studies, little data exists on measuring anxiety during the first few weeks following medically assisted withdrawal, or how anxiety affects treatment and relapse during this critical time in residential treatment. The aims of this study were to determine whether (1) patients who fail to complete residential treatment differ in level of anxiety symptoms on admission from those who complete treatment (2) patients who relapse, or leave residential treatment prior to completion, have higher anxiety scores prior to discharge than individuals who complete treatment, (3) self-report of PTSD symptoms affects change in anxiety symptoms during the first 60 days of substance abuse recovery, and (4) reported PTSD is a significant factor in drop-out from residential treatment prior to completion.

Methods: A prospective study was conducted with 53 males entering a residential program immediately following medical detox from alcohol or opiates. A one group repeated measures design was used with anxiety data (Zung SAS) collected at entry, 30, and 60 days.

Results: While the relationship between Zung anxiety scores on admission and leaving treatment were not significant (p-value =.96), there was a significant difference between the last measured anxiety score and leaving treatment prior to completion (p-value $\leq$ .02) when compared to

treatment completers. While not significant, there was a trend in the slowing of the rate of anxiety diminishing in those with PTSD symptoms and those without ($p > .08$). However, men with PTSD did not leave treatment prior to completion more frequently than those without PTSD.

Conclusion: Anxiety is a significant factor in relapse during the first two months of treatment. Individuals with persistent anxiety were less likely to complete treatment than those whose anxiety remitted during the first few weeks after detox. Reported PTSD was not an independent risk factor in leaving treatment prior to completion.

Introduction

Empirical evidence suggests that most individuals will have significant anxiety during the initial weeks of treatment and early recovery from opiate and alcohol dependence (Schuckit & Hesselboch, 1994, Sher, 2002). Stress and anxiety have been identified as high risk reasons for relapse (Levy, 2008). Anxiety is a common co-occurring disorder in substance abusers (Smith & Book, 2008) and a multisystem response to a perceived threat or danger, generally produced by somatic symptoms in the present and cognitively by anticipation of stressful events in the future. It is the most prominent negative emotional state which many patients endure during the post-acute withdrawal period immediately following medical detox (Colasanti, Rabiner, Lingford-Hughes, & Nutt, 2010, McGuinness & Fogger, 2006).

The anxiety symptoms commonly associated with substance abuse withdrawal during the first few weeks of abstinence are characterized by insomnia (Monti & Monti, 2000, Thakker 20011), generalized irritability (Koob & Le Moal, 2005), low distress tolerance (Daughters,

,Lejuez, Kahler, Strong, & Brown, 2005), difficulty with cognitive processing (Eysenck, Derakshan, Santos & Calvo 2007) and exacerbated by hypersensitivity to pain (Vachon-Presseau et al., 2013). The amount and duration of these anxiety symptoms during this post-acute withdrawal period reflect a variety of neurochemical changes in the body, the extent of which are manifested by the individual's personality, life experiences and genetic makeup (Nemeroff, 1998), as well as the type and amount of preceding drug use.

During the post-acute withdrawal period, many anxiety symptoms abate without treatment (DSM-5) over 3 to 6 weeks. It is not known whether acute anxiety symptoms in the immediate post withdrawal period abate at a different rate in men who endorse symptoms of Post Traumatic Stress Disorder (PTSD) than in those who do not (Gil-Rivas, Prause, & Grella, 2009). Nor have studies addressed whether a high level of anxiety during the first week following detox is a risk factor for relapse over the next two months. However, it is known that the risk of relapse due to anxiety, when present, persists far beyond these first two months in recovery (Heilig, Elgi, Crabbe, & Becker, 2010). In a prospective study of substance abusers in recovery (Charney, Palacios-Boix, Negrete, Dobkin, & Gill, 2005), 48% presented with anxiety during the immediate post withdrawal period. Of these, only 40% of them were abstinent at 6 months. This evidence suggests that increased anxiety at intake is a predictor of treatment outcome.

The negative effect of lifetime trauma such as childhood abuse (Elliot et al., 2014) has also been identified as an increased risk factor associated with relapse and continued substance abuse (Lejuez et al., 2008, Darke, 2013). In a convenience study of male substance abusers (Gil-Rivas et al., 2009), 73% had a preexisting diagnosis of mood disorder, and 52% had a life time diagnosis of PTSD. Almost 27% admitted to a lifetime history of opiate dependence and more

than 70% to alcohol dependence. Anxiety was measured at three time points: within 48 hours of admission, at 3 months and at 12 months. Anxiety was highly correlated between all the time points ($r = .71$, $P < .001$). Relapse rates of 45.3 % at 3 months and 52.6% at 12 months were identified in those with PTSD. Anxiety symptoms did not decrease between 6 and 12 months after start of treatment.

Effect of Treatment on Anxiety

Relieving anxiety, and the commonly associated somatic symptoms, as well as addressing the psychosocial components of addiction, are paramount for maintaining patients in treatment and reducing dropout and relapse. In early recovery, the inability to attend to what is being taught also increases the risk of relapse during this initial period because learning coping skills and increasing self-efficacy are critical components of recovery. Anxiety has been shown to decrease attention and ability to successfully complete tasks. Studies have confirmed this in alcoholics in early recovery (Daughters et al., 2005). A study in college students (Chapell et al., 2005) also identified that with increased anxiety, comprehension in learning new material decreases.

A meta-analysis of anxiety and its relationship to performing creative tasks, suggested that there is a significant negative relationship between increase in anxiety and the ability to complete verbal tasks ($p < .001$) (Byron & Khazanchi, 2011). When individuals devote more cognitive resources to their anxiety and its symptoms, less personal resources are available for creative expression. Anxiety is also a component of low distress tolerance (Keough, Riccardi, Timpano, Mitchel, & Schmidt, 2010). Daughters et al. (2005) addressed the impact of low distress tolerance in substance abusers during early recovery ($n = 89$, 62% male, almost 90%

alcohol or poly substance abusers, 80% high school or less) in a period of 6 weeks of inpatient treatment. A significant reduction in task completion was noted ($r = .27$), ($p = .01$) between those participants who were tested more closely to (1-2 weeks post) detox when compared to those who were tested 5 to 6 weeks post-detox.

Anxiety in Integrative Treatment

An integrative approach to substance abuse treatment which focuses on enhancing coping skills, relapse prevention, psycho-education and 12 step programs, as well as psychotherapy in individual sessions for both the substance abuse and concurrent mental health disorders has been supported for many years (Miller, Sorensen, Selzer, & Brigham, 2006). Hesse (2009) in a systematic review focusing on anxiety and depression in substance use treatment, found some support for integrated psychotherapy in the treatment of depression and substance abuse. However, due to a paucity of similar studies, a meta-analysis was unable to be completed on anxiety during substance abuse recovery treatment. Five studies were identified, which met criteria, but measurement methods were dissimilar. In these studies there was little evidence to suggest that non-somatic or specialized treatment of anxiety disorders yielded any significant benefit during early recovery. However, there was a recommendation that more research was needed in this area (Hesse, 2009). Therefore, the purpose of this study was to identify the level of anxiety experienced by men in early recovery in an integrative substance abuse program.

The aims of this study were to determine whether (1) patients who fail to complete residential treatment differ in level of anxiety symptoms on admission from those who complete treatment, (2) patients who relapse, or leave residential treatment prior to completion, have higher anxiety scores prior to discharge than individuals who complete treatment, (3) self-report

of PTSD symptoms affects change in anxiety symptoms during the first 60 days of substance abuse recovery, and (4) reported PTSD is a significant factor in drop-out from residential prior to treatment completion.

Method

Design

This study used a one group repeated measures design with anxiety data collected at entry, 30 days, 60 days, and at discharge. Symptoms of PTSD were measured at intake and correlated with anxiety measures at each time point.

Setting

The setting for this study was a Level II residential treatment program operated by the Center for Drug Free Living (CFDFL) and certified by the Commission on Accreditation of Rehabilitation Facilities. This Level II program provided up to 6 hours of psychosocial support daily in a structured environment. The treatment program included daily group sessions with psychoeducation, treatment with psychopharmaceuticals as needed, as well as weekly individual counseling. This model of integrated treatment is the present standard of care for substance abuse treatment. All residents admitted to the Level II program were referred directly from the associated detox facility. The average length of stay in the program was 60 days but varied from 30 to 90 days.

Enrollment and Duration of Study

A total of 53 men who met study criteria of either opiate or alcohol dependence were enrolled over 12 weeks between 1 January 2012 and 5 May 2012. Each participant had completed either an opiate (63%, n = 33) or alcohol (37%, n = 20) medical detox in the week prior to admission.

Required Sample Size

Attrition rate was 26 % resulting in a sample of analysis of 39 at 30 days of treatment. Assuming a power of .80 and an alpha of .05, a sample of 39 was sufficient to detect a moderate effect.

Procedures

The study was discussed with all potential participants by the principal investigator (PI) at the Detox facility's weekly community meeting. Participants were recruited on arrival at the residential treatment facility and 53 participants were enrolled. Within 48 hours of arrival at the program, the PI met with interested clients, obtained informed consent and gave the client a copy of the signed consent. The participants then completed the entry demographic questionnaire and the PTSD Checklist –Civilian version (PCL-C). Participants also completed the baseline anxiety (Zung SAS) inventory during a clinical interview with the PI on the same day study enrollment was completed. On day 28-30 and on day 55-60 of the program, the participants completed the Zung SAS again if they were still enrolled in treatment. Participants remaining in residential treatment also completed the final Zung SAS at 90 days (n = 3). If participants did not wish to be contacted, or left without notice, this was noted on the discharge or final questionnaire and

participation in the study was terminated. The PI gave all the participants who completed the study a $10 gift card to a local super market or super store at the time of their final data collection.

Study measures

Demographics: A demographic questionnaire was used to assess age, education, race/ethnicity, housing situation prior to admission, primary substance of abuse and mental health disorders prior to admission. Medications being taken on admission and at 30 days were obtained from the medical record.

Anxiety: Anxiety experienced over the past few days was measured using the Zung SAS. This 20 item self-administered anxiety scale is used for identifying somatic and psychological anxiety symptoms that have occurred within the past few days. Each item is scored as a 4 point Likert scale with 5 items being reverse scored. Anxiety scores between 45 and 60 are considered moderate anxiety, and scores between 60 and 74 are considered severe anxiety. A raw score of > 36 is clinically significant for difficulty carrying out normal work or activities (Zung, 1980). The Zung score (Zung, 1971) has good reliability (r = .71, alpha = .798) and content validity when compared to the Hamilton Anxiety scale (r =.75. Zung, 1971). The Zung scale has been used in various populations for research and clinical assessment since its development in 1971 (Sharpley & Christie, 2007, Liao et al.2011).

PTSD: The PTSD Checklist—Civilian Version (PCL-C) was used to assess for symptoms of PTSD. This self-administered instrument has been in general use for more than 20 years in both military and civilian populations (Orsillo, 2001). Scores of less than 29 are considered not significant for PTSD, while those above 45 are considered of high enough

severity for continuing with the assessment for the diagnosis of PTSD. The PCL consists of 17 items identified with the diagnosis of PTSD in the DSM, and uses a 5 point Likert scale. Internal consistency is high (r = .75) across studies in various populations (Wilkins, Lang & Norman, 2011).

Data Analysis

Descriptive statistics (e.g. mean, S.D., frequency and %) were calculated on demographic variables and included presence or absence of PTSD symptoms. The key study variables of anxiety and treatment completion were also compared between the group who reported PTSD symptoms and the group who did not. Research questions were answered using Pearson r correlation or t-test to identify differences in the anxiety scores between time periods.

Results

All 53 participants completed the baseline data collection. Two participants (3.7%) left treatment within the first week, and an additional 3 (5.6%) left the second week. At 30 days, a total of 13 (24.1%) were no longer in treatment. Three were discharged after successful completion and 10 left without notice or were discharged due to drug use on property (18%). Only 3 were available to complete a final anxiety inventory at 90 days. A total of 15(28.3%) participants dropped out of treatment prior to completion.

Fifty-three participants completed baseline data and were between the ages of 18 and 63, with a majority (>70%) between ages 25-50 years. The majority of participants self- identified as white, homeless or lived with friends, and were educated at the high school level or higher (see Table1). Forty-nine percent (n=17) reported poly substance use with opiates and 38% (20)

were previously diagnosed with a mental health disorder. High levels of anxiety were reported in 34% (n=18) of participants. A score of >30 on the PCL was noted on 84% (n=48) of men and 43% (n=23) reported PTSD symptoms in the high range (>50).

Table 5: Population demographics on admission

	Male (n= 53)
Age group [n (%)]	
Less than 25	6 (11.3%)
26-35	14 (26.4%)
36-50	24 (45.3%)
Over 50	9 (17.1%)
Race/Ethnicity [n (%)]	
European/White	36 (67.9%)
Hispanic	12 (22.6%)
African American	2 (2.5%)
Living situation prior to treatment [n(%)]	
Family or self	15 (28.3%)
Living with parents	7 (13.2%)
Transitional housing or friends	8(15.1%)
Homeless	23 (43.4%)
Years of Education	
< High School	9 (17.0%)
GED	9 (17.0%)
HS Diploma	16 (30.2%)
college/trade/AA	19(33.8%)
Primary Substances of Abuse [n (%)]	
Opiate only	16 (13.2%)
Alcohol only	20 (37.7%)
Poly substance with opiate	17 (49%)
Mental Health Disorders (pre admission)	20 (37.7%)
Zung less than 37 -low anxiety [n (%)]	16 (30.2%)
Zung greater than 50 – high Anxiety [n (%)]	18 (34.0%)
PCL greater than 50 –High [n (%)]	23 (43%)
PCL greater than 40 Med (n (%)}	40 (75%)
PCL greater than 30 Low [n (%)]	48 (84.2%)

Anxiety scores were consistent with empirical evidence which identifies a sharp decrease in anxiety by 30 days post detox with a general flattening of anxiety symptoms in the following 30 days (Table 2). The correlation between scores on admission and scores at 30 days (r = .59) and 60 days (r = .64) was strong.

Table 6: Anxiety scores at three time points

	Admission	30 day	60 day
N =	53	39	21
Mean (SD)	43.6(12.0)	34.5(8.7)	35.9(12.2)

The difference between anxiety level at admission and completing or leaving treatment early was not significant ($p \geq .96$). There was a significant difference ($t=2.36$; $p \leq 02$) between last anxiety score collected and leaving treatment early. Participants who left treatment early reported higher anxiety.

There was a positive correlation between endorsement of PTSD symptoms (PCL-C greater than 30) and endorsement of anxiety symptoms (Zung SAS) on admission (r = .49) Correlation was even greater with a PCL greater than 50 (r = .54). While not significant, a trend in the slowing of the rate of anxiety diminishing in those with PTSD symptoms and those without ($p > .08$) was evident. However, men with PTSD did not leave treatment prior to completion more frequently than those without PTSD.

Discussion

Elevated anxiety symptoms in patients leaving treatment prior to completion of treatment was found to be more significant than the level of anxiety participants reported on admission to residential treatment following medical detox. Anxiety associated with the common symptoms of alcohol and opiate withdrawal usually remits within 3-6 weeks (Brady, Haynes, Hartwell, & Killeen, 2013). Hence there has been less interest in research treatment during this period although more than 25% of clients admitted to treatment drop out during this period. Although patients with self-reported PTSD symptoms had a slightly slower rate of anxiety symptoms diminishing, it did not affect their length of time in treatment. Whether the PTSD was childhood or adult onset, which may have been a variable, was not measured.

Factors within an integrative program may also contribute to continued anxiety during residential treatment. High social anxiety was identified as a predictor of early drop-out, especially in recovery programs, where much group work was expected (Lejuez, et al. 2008). Low distress tolerance (Daughters et al 2005) and high anxiety sensitivity (Lejuez, et al. 2008) may also contribute to sustained anxiety in a residential setting where task completion and group participation is expected. The impact of PTSD and its association with substance abuse is well recognized. Gil-Rivas et al. (2009) noted that more than 45% of patients with PTSD in recovery relapsed within 3 months. Therapy involving previous life trauma may increase anxiety (Kelly & Daley, 2013). Individual trauma is often addressed in both individual therapy as well as in groups and is viewed as a necessary step in recovery treatment (Smith & Book, 2008). An individual who has difficulty dealing with these thoughts and emotions may also have increased anxiety which could contribute to early dropout.

The presence and effect of other preexisting anxiety disorders must also be considered, and when recognized, treated (Kelly & Daley, 2013). Almost 50% of patients with substance use disorders have self-reported generalized anxiety starting in late adolescence or earlier. This is usually the rationale used for their addictive disorder, often described as self-medication (Darke, 2013). It is also well documented in history that alcohol and opiates have been used for millennia to reduce anxiety and associated stress symptoms and is the most effective coping mechanism these individuals have developed. When anxiety becomes intolerable, persons with addictive disorders revert to behavior which brings relief (Brady, Haynes, Hartwell, & Killeen, 2013). This is relapse which was identified as the most common reason for participants leaving treatment early in this study. Anxiety stemming from these underlying causes is much less likely to remit during the early weeks of recovery than anxiety associated with the common symptoms of alcohol and opiate withdrawal (Brady et al., 2013).

This study addressed the symptoms of anxiety in early recovery. Relief of anxiety during this period is critical for enhancing learning and building coping skills. It is well recognized that the longer an individual stays in treatment, the better his chances of remaining in recovery (McLellan & McKay, 2003). However in the present day managed-care environment, 30 days is usually the maximum allowed time for residential treatment. This research study presents an argument for identifying and initiating treatment for underlying anxiety disorders early in the recovery process, as well as treating associated somatic complaints. This will allow for maximum use of time in treatment to develop the internal tools and lifestyle changes needed to enhance potential for recovery.

Limitations

This was a focused study of anxiety in men at a single residential recovery program. With the exception of PTSD symptoms, related variables were not considered. These include depression which is highly correlated with anxiety but was not measured in this study, as well as a history of childhood trauma. The psychotherapy method used by individual therapists or case managers was not identified, nor was the depth of the therapeutic relationship, both of which could have impacted level of anxiety. The study was underpowered and limited to individuals with primary alcohol or opiate use disorders. However, many were poly-substance abusers and also may have had other medical or mood disorders which could have affected outcomes in a larger study. Of interest, most participants who left the residential program early were unavailable to complete follow up anxiety scales and were unwilling to complete questionnaires prior to leaving. Contact phone numbers had often been disconnected or the individual answering the phone was unaware of the participant's whereabouts. Anecdotally, many of the participants returned to detox in the following months and related their stories regarding relapse.

Conclusion

Anxiety is a significant factor in relapse during the first months of substance abuse recovery. Individuals with persistent anxiety are less likely to complete treatment than those whose anxiety remits during the first few days or weeks after detox. Post-Traumatic Stress Disorder is a significant variable in substance abuse and in this study it appears that it may influence the course of anxiety symptom degradation.

Recommendations

More research is needed to identify methods of decreasing and sustaining decreases in anxiety very early in recovery in order to enhance program retention and ultimately maintain substance abuse recovery. There is a need for more study on the integration of psychotherapy such as motivational interviewing and non-sedating pharmacotherapy such as long acting naltrexone as a means to decrease anxiety during the initial weeks of treatment. This is the time when anxiety peaks and dropout from treatment is most likely. Early interventions are critical for enhancing learning and sustaining desire for recovery through decreasing anxiety symptoms and so enabling the substance abuser to apply the adaptive behaviors learned in therapy to their own lives. Complementary and alternative medications/treatments (CAM), as well as somatic therapies now being researched, may also have a role in decreasing anxiety without the sedating effect often seen with psychopharmacotherapy. Individualized treatment should also include genetic testing for identifying sensitivities to medications. This would assist in prescribing the most likely effective pharmacotherapy for the individual early in treatment.

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APPENDIX A: IRB APPROVAL CHAPTER 3

University of Central Florida Institutional Review Board
Office of Research & Commercialization
12201 Research Parkway, Suite 501
Orlando, Florida 32826-3246
Telephone: 407-823-2901 or 407-882-2276
www.research.ucf.edu/compliance/irb.html

Approval of Human Research

From: UCF Institutional Review Board #1 FWA00000351, IRB00001138

To: **Janet M. Hutchison**

Date: **June 20, 2013**

Dear Researcher:

On6/20/2013 the IRB approved the following human participant research until 5/21/2014 inclusive:

Type of Review:	Submission Correction for UCF Initial Review Submission Form Full Board Review
Project Title:	Using Cranial Electrotherapy Stimulation to Decrease Anxiety Symptoms following Opiate and Alcohol Withdrawal
Investigator:	Janet M. Hutchison
IRB Number:	SBE-13-09325
Funding Agency:	Electromedical Products International, Inc | 2201 Garrett Morris Parkway | Mineral Wells | TX | 76067(EPI), International Nurses Society on Addictions(INTnsa)
Grant Title:	
	N/A
Research ID:	
	N/A

The scientific merit of the research was considered during the IRB review. The Continuing Review Application must be submitted 30days prior to the expiration date for studies that were previously expedited, and 60 days prior to the expiration date for research that was previously reviewed at a convened meeting. Do not make changes to the study (i.e., protocol, methodology, consent form, personnel, site, etc.) before obtaining IRB approval. A Modification Form **cannot** be used to extend the approval period of a study. All forms may be completed and submitted online at https://iris.research.ucf.edu .

If continuing review approval is not granted before the expiration date of 5/21/2014, approval of this research expires on that date. When you have completed your research, please submit a Study Closure request in iRIS so that IRB records will be accurate.

Use of the approved, stamped consent document(s) is required. The new form supersedes all previous versions, which are now invalid for further use. Only approved investigators (or other approved key study personnel) may solicit consent for research participation. Participants or their representatives must receive a signed and dated copy of the consent form(s).

In the conduct of this research, you are responsible to follow the requirements of the Investigator Manual.

On behalf of Sophia Dziegielewski, Ph.D., L.C.S.W., UCF IRB Chair, this letter is signed by:

Signature applied by Patria Davis on 06/20/2013 11:32:58 AM EDT

IRB Coordinator

APPENDIX B: IRB CONSENT CHAPTER 3

University of Central Florida

Using Cranial Electrotherapy Stimulation to Decrease Anxiety Symptoms following Opiate and Alcohol Withdrawal

Informed Consent

Principal Investigator: Janet Hutchison, MSN

Faculty Supervisor: Anne Norris, PhD

Investigational Site: Center for Drug Free Living, Orlando, Florida

Sponsor(s): The International Nurses Society on Addictions, and Electromedical Products International, Inc.

Introduction: Researchers at the University of Central Florida (UCF) study many topics. To do this we need the help of people who agree to take part in a research study. You are being invited to take part in a research study which will include about 78 men who are starting on the road to recovery from an addictive disorder. You have been asked to take part in this research study because you are in a residential treatment and you are 18 years of age or older.

The person doing this research is Janet Hutchison, a Nurse Practitioner at the Center for Drug Free Living, and a PhD student in the College of Nursing at the University of Central Florida. Dr Anne Norris, a UCF faculty supervisor in the College of Nursing is supervising this project because Janet is a PhD student.

What you should know about a research study:

- Someone will explain this research study to you.
- A research study is something you volunteer for.
- Whether or not you take part is up to you.
- You should take part in this study only because you want to.
- You can choose not to take part in the research study.
- You can agree to take part now and later change your mind.
- Whatever you decide it will not be held against you.

- Feel free to ask all the questions you want before you decide.

Purpose of the research study:

The purpose of this study of anxiety during post-acute withdrawal from opiates and alcohol is to identify whether cranial electrotherapy stimulation (CES) therapy (Alpha wave stimulation) is an effective treatment for the relief of anxiety symptoms during the first month of substance abuse recovery [illegible] treatment.

CES is believed to reduce anxiety symptoms through a low level of pulsed alpha wave current which affects some of the neurotransmitters in the brain and ultimately reduces stress. It is approved by the U.S. Food and Drug Administration ([FDA] 2011) for use in the treatment of anxiety as well as depression and sleep disorders. The device used in this study is a commercial unit brand named 'alpha stim'.

What you will be asked to do in the study:

You will be asked wear the CES device that has been assigned to you for an hour each day during the study period. Half of the men in this study will be using a unit that transmits a low level of pulsed alpha waves. The other half will wear a unit that does not transmit any alpha waves. You will not be able to choose which group you are in. Neither you nor Janet, the Investigator, will know whether you have an active or an inactive unit until after the entire study is complete. This is known as a double blinded study.

You will not be able to adjust any settings. You might feel a slight tingling sensation when the device is activated, however, many people do not and it is not necessary to feel anything for the intended effect to occur.

- Today you will be asked to fill out a short questionnaire about your life, drug use and medical or mental health problems you may have.
- You are also being asked to allow me (Janet) to review your medical record to collect the names and dosages of medications you are taking while you are in this study as study data.
- You will also fill out a short form with some questions about feelings you may have. This questionnaire is called the Zung SAS and measures anxiety.
- You will also be able to discuss more information about Cranial Electrotherapy Stimulation (CES) and have an opportunity to look at the device and ask questions regarding how it works and be shown how to wear the device and apply the ear pieces.
- The study intervention will involve wearing the CES device for one hour each day (in the morning) during your first three weeks in residential treatment, for a total of 15 sessions. Usually the CES device will not be used on weekends. The devices will be kept in the nursing office or with a designated counselor. The device will have your name on it and is to be used only by you.

- On the 1st and 15th session of CES treatment, you will collect saliva samples in the morning, within 30 minutes before and after the CES treatment on that day. The saliva will be used to measure your cortisol level. (The specimen samples will only measure cortisol and will be destroyed after the testing at the Laboratory is completed). On these days only, you will be asked to refrain from brushing your teeth, eating, drinking or smoking for the hour prior to cortisol collection. You may wear a nicotine patch if desired.
- When you collect the cortisol samples, you will also fill out another short anxiety questionnaire called the STAI-6.
- When you have been in residential treatment for 30 days, the Investigator will ask you to complete the Zung Anxiety questionnaire as well as questionnaires about PTSD (the PCL-C) and Depression (the PHQ). This will end your participation in the study.
- Janet or her assistant will give you a $5 gift card after completing the 2nd cortisol specimen following the first session of CES treatment, and a $10 gift card to Target or Walmart at the end of the study after you complete the final questionnaires when you have been in residential treatment for 30 days. The total compensation to you for this study will be $15 in gift cards.
- If you need to speak to Janet regarding any medical or mental health concerns you are having, you may discuss them with her at regularly scheduled appointments times, or after completion of the questionnaires. This will not affect your participation in the study.

Location: All data collection and questionnaire completion related to the study during residential treatment will be done in the nurse's office or another private office in the facility.

Time required: We expect that you will be in this research study for 1 month.

The first appointment, including this visit, may take up to an hour. However, the study questionnaires you complete after that first appointment are short and only take a few minutes to complete. The treatment with the CES will take about an hour and a half daily, including picking up and applying the electrodes and returning it to the office each day, but you will wear the device during a morning group and it will not interfere with normal activities. You will wear the device for a total of 15 daily sessions during the first 3 weeks of residential treatment. On the days when the cortisol is collected, an additional 30 minutes will be needed. This should not interfere with group participation or any other activities in the residential program. On the final day of the study, it may take you up to an hour to complete the questionnaires.

Funding for this Study: This research study is being paid for in part by the (International Nursing Society for Addictions) and by the manufacturer of the alpha stim® CES device; Electromedical Products International, Inc. This funding will pay for the collection and measurement of the cortisol and other expenses associated with the study.

Risks: Adverse effects when using alpha stim® are usually mild and self-limiting. In 4500 patients who used alpha stim® there were 6 cases of dizziness (0.13%), 5 cases of skin irritation (0.11%), and 9 cases of headaches (0.20%). In this research, the current level is set at a low dose and the device

automatically shuts off after one hour of use to keep you from having any dizziness or burning/skin irritation. There have also been isolated reports of blood pressure being lowered when CES is used. If you are on a blood pressure lowering medication, this will be monitored. Paradoxical reactions such as hyper excited states and increased anxiety have occasionally occurred so if this happens, you need to tell Janet or a staff member at the Center for Drug Free Living.

It is also possible that in completing the PCL-Civilian you may be uncomfortable with remembering traumatic events. If this occurs, you will have access to nurses and counselors with whom you can discuss these feelings should they arise.

While it is possible that you may experience anxiety while completing the Zung SAS, the STAI-6 or the PHQ-9, this seems unlikely as these are the same questionnaires are routinely used in community primary care. If this occurs you would need to let Janet or your counselor know.

Benefits: We cannot promise any benefits to you or others from your taking part in this research. However, the FDA has approved the use of this device in the treatment of anxiety, depression and insomnia. We hope that you will feel informed and reassured by the conversations that study participation will create. Choosing to participate in this study will have no effect on your treatment if you are enrolled in treatment under a court order, nor will the court be aware that you are involved in this research study.

Liability: UCF is not liable for any adverse events that may occur related to your participation in this study

Compensation or payment: Compensation for your participation will be $15 in gift cards for either Target or Walmart. Janet or her assistant will give you a $5 gift card after completing the cortisol collections on the first day of the study and a $10 gift card to Target or Walmart at the end of the study after you complete the final questionnaires when you have been in residential treatment for 30 days.

Confidentiality: We will limit your personal data collected in this study to people who have a need to review this information. Only Dr Norris and the Institutional Review Board will be able to access this information. However, they would not have access to your name, only information identified with a number. If, while you are filling out questionnaires you make any remarks that are interpreted as being harmful to yourself or others, it will be disclosed to the appropriate authorities, but you will be informed and involved in this process. Only Janet will have access to your medical record to confirm information needed for the study. Once your part of the study is completed, any information about you will be 'deidentified' and will not be able to be traced back to you.

The Saliva specimens will be used for measurement of cortisol only and will not have any personal identifying information submitted to the laboratory with the specimen. The specimens will be destroyed by the laboratory after 30 days.

If you have been court ordered into treatment, information about your participation in this study will not be released to the courts. Nor will information about your study participation be released to anyone else. Participation in this study is entirely voluntary and confidential.

Study contact for questions about the study or to report a problem: If you have questions, concerns, or complaints, or think the research has hurt you, please talk to the Principal Investigator, Janet Hutchison. You may call her at 407-267-0400. You may also contact Dr. Anne Norris, Faculty Supervisor, College of Nursing, by email her at anorris@ucf.edu .

IRB contact about your rights in the study or to report a complaint: Research at the University of Central Florida involving human participants is carried out under the oversight of the Institutional Review Board (UCF IRB). This research has been reviewed and approved by the IRB. For information about the rights of people who take part in research, please contact: Institutional Review Board, University of Central Florida, Office of Research & Commercialization, 12201 Research Parkway, Suite 501, Orlando, FL 32826-3246 or by telephone at (407) 823-2901. You may also talk to them for any of the following:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You want to get information or provide input about this research.

Withdrawing from the study: You may withdraw from the study at any time. There are no consequences to doing this. If you are in treatment under a court order, this is not reported to the courts, or to your counselor. If you decide to leave the study, contact the investigator so that the investigator can remove your information from the study if that is your wish. If you leave the treatment program prior to study completion, the information already collected may be used in the study, unless you request that the information be removed. The person in charge of the research study (Janet) can also remove you from the research study without your approval. Possible reasons for removal include not being able to complete the daily CES treatment or the cortisol collections. Janet may also remove you from the study if she feels that continuing in the study is not in your best interest.

HIPPA: Information from your medical record to be used in this study will be limited to what medications you are taking during the period of study participation and the number of times you visited Janet to discuss symptoms related to withdrawal or your mental health (Attachment 1).

Your signature below indicates your permission to participate in this research. ***and to the use and disclosure of your protected health information:***

DO NOT SIGN THIS FORM AFTER THE IRB EXPIRATION DATE BELOW

Name of participant	
Signature of participant	Date
Signature of person obtaining consent	Date

VOID

Printed name of person obtaining consent

Attachment 1

Research Consent Form Addendum: Authorization to Access Personal Health Information (PHI) under the Health Insurance Portability and Accountability Act (HIPPA).

Introductio
As part of yo par ipation in the research study, 'Using Cranial Electrotherapy Stimulation to Decrease An ty ymptoms following Opiate and Alcohol', described in the attached consent form, the Principal In igator, Janet Hutchison, MS, ARNP is seeking your permission to access personal health information (PHI) through which you can be identified, which is contained in your medical/clinical records at the Center for Drug-Free Living.

The PHI that we are requesting authorization to access is as follows: information about medications you may be taking during the time that you are in this study, as well as the number of times you visited Janet to discuss withdrawal symptoms or mental health problems.

All records containing your per nal infor ation, whether research or medical/clinical, will be kept secure and confidential. The a ached co ent form for the research study describes the confidentiality of your research cords. his authorization form describes how PHI from your medical/clinical records, if neede will e disclosed to the research team.

Purpose
This information will be used by the researcher to conduct the research study. The Principal Investigator will have access to your PHI for purposes of the study. Except as described in the consent form, no one else will have access to your PHI.

Additional Information

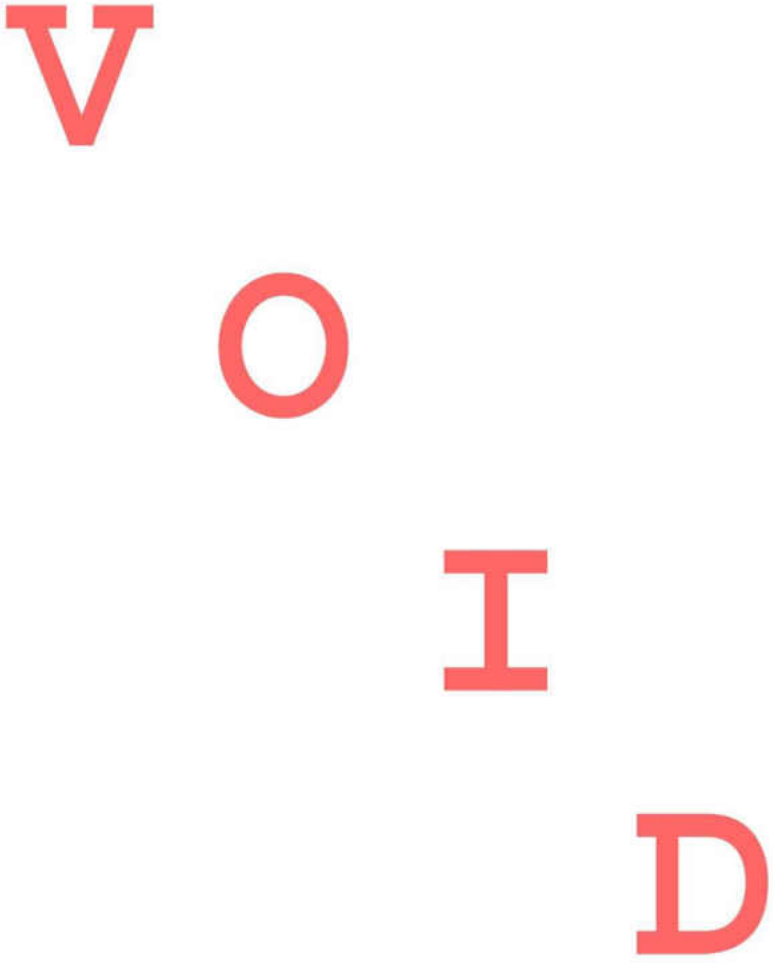
- This authorization will continue until the end of the esearch study. You may withdraw this authorization for the researcher to access and us your PHI at any time by contacting the Principal Investigator, in writing, at Janet Hutchiso The Center for Drug-Free Living, 100 West Columbia St, Orlando, FL 32806. If you withdraw your authorization the researchers may continue to use the information they have already collected. If you withdraw your authorization you will not be able to continue participation in the research.
- If you do not wish to authorize access to your PHI, it will not be possible for you to participate in the study. It will not affect your continuing treatment at the Center for Drug-Free Living.
- Information provided to the research team will become part of the records and will continue to be covered by the HIPAA Privacy Regulations while kep by the enter for Drug-Free Living. However, you should be aware that information disclos d by th esearch team to any other person or institution specified in the attached consent f m may o longer be covered by the HIPAA Privacy Regulations.
- You will be given a signed copy of this authorization.

Signature and Authorization
I authorize the release of my medical/clinical records as described above.

Print Name

Signature

Date: ___ ___ / ___ ___ / ___ ___ ___ ___



APPENDIX C: IRB APPROVAL CHAPTER 4

University of Central Florida Institutional Review Board
Office of Research & Commercialization
12201 Research Parkway, Suite 501
Orlando, Florida 32826-3246
Telephone: 407-823-2901 or 407-882-2276
www.research.ucf.edu/compliance/irb.html

Approval of Human Research

From: **UCF Institutional Review Board #1**
FWA00000351, IRB00001138

To: **Janet M Hutchison**

Date: **December 16, 2011**

Dear Researcher:

On December 16, 2011, the IRB approved the following human participant research until 12/15/2012 inclusive:

Type of Review:	UCF Initial Review Submission Form Expedited Review Category #7
Project Title:	Measuring Anxiety Post Detox in Residential Treatment
Investigator:	Janet M Hutchison
IRB Number:	SBE-11-08039
Funding Agency:	None

The Continuing Review Application must be submitted 30days prior to the expiration date for studies that were previously expedited, and 60 days prior to the expiration date for research that was previously reviewed at a convened meeting. Do not make changes to the study (i.e., protocol, methodology, consent form, personnel, site, etc.) before obtaining IRB approval. A Modification Form **cannot** be used to extend the approval period of a study. All forms may be completed and submitted online at https://iris.research.ucf.edu .

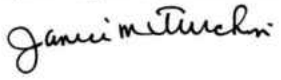
If continuing review approval is not granted before the expiration date of 12/15/2012, approval of this research expires on that date. When you have completed your research, please submit a Study Closure request in iRIS so that IRB records will be accurate.

Use of the approved, stamped consent document(s) is required. The new form supersedes all previous versions, which are now invalid for further use. Only approved investigators (or other approved key study personnel) may solicit consent for research participation. Participants or their representatives must receive a signed and dated copy of the consent form(s).

In the conduct of this research, you are responsible to follow the requirements of the Investigator Manual.

On behalf of Sophia Dziegielewski, Ph.D., L.C.S.W., CF IRB Chair, this letter is signed by:

Signature applied by Janice Turchin on 12/16/2011 02:40:53 PM EST



IRB Coordinator

APPENDIX D: IRB CONSENT CHAPTER 4

University of Central Florida

MEASURING ANXIETY POST DETOX IN RESIDENTIAL TREATMENT

Informed Consent

Principal Investigator(s): Janet Hutchison, MSN

Sub-Investigator(s): None

Faculty Supervisor: Anne Norris, PhD

Investigational Site(s): Center for Drug Free Living, Orlando, Florida

Introduction: Researchers at the University of Central Florida (UCF) study many topics. To do this we need the help of people who agree to take part in a research study. You are being invited to take part in a research study which will include about 80 people who are starting on the road to recovery from an addictive disorder. You have been asked to take part in this research study because you in a recovery treatment program. You must be 18 years of age or older to be included in the research study.

The person doing this research is Janet Hutchison, a Nurse Practitioner at the Center for Drug Free Living, and a PhD student in the College of Nursing at University of Central Florida. Because the researcher is a PhD student, she is being guided by Dr Anne Norris, a UCF faculty supervisor in the College of Nursing

What you should know about a research study:

- Someone will explain this research study to you.
- A research study is something you volunteer for.
- Whether or not you take part is up to you.
- You should take part in this study only because you want to.
- You can choose not to take part in the research study.
- You can agree to take part now and later change your mind.
- Whatever you decide it will not be held against you.
- Feel free to ask all the questions you want before you decide.

Purpose of the research study: The purpose of this study is to see how anxiety affects the progress someone in early recovery from a substance use disorder, makes towards long term recovery. It will also measure if there are certain times in early recovery when anxiety will be either better or worse.

What you will be asked to do in the study:

- Today you will be asked to fill out a short questionnaire about your life, drug use and medical or mental health problems you may have.
- You will also fill out a short form with some questions to see if you may have Post Traumatic Stress Disorder (PTSD).
- You will be asked to complete another questionnaire about feelings you may have which are related to anxiety. This questionnaire will be completed either after this meeting or during the next few days. This questionnaire, called the Zung SAS, is computer based on an internet site. The internet site cannot trace your answers back to you. The results will be explained to you and written in your medical record. The results will not be saved on the computer.
- Every 4 weeks while you are in the recovery treatment program, the investigator will ask you to take the same anxiety questionnaire and the results will be explained to you. These following questionnaire results will not be put in your medical record, only in your research study file.
- You will be asked to take the anxiety questionnaire before you leave the program and also fill out a short questionnaire about leaving the program.
- We will also want to contact you by telephone or email, some weeks after you leave the program and have you take the anxiety questionnaire again and also fill out a very short questionnaire about how your life is going. The principle investigator will set up meeting with you. If you cannot meet, the meeting may be done by telephone.
- After you finish this last questionnaire, you will receive your choice of a $10 gift card to Target, Wal-Mart or Publix.

Location: All interviews and questionnaire completion during residential treatment will be done in the nurse's office or another private office in the facility. At the three month interview, the investigator will meet you in a public place such as a coffee shop, or at Outpatient Services if you are still enrolled in treatment. If you have moved out of the area, the appointment may be done by telephone.

Time required: We expect that you will be in this research study for about three months: Once a month, during the time that you are in treatment you will meet with the investigator. She will also meet with you at the time you are discharged from the program, and then have one additional visit with the investigator about a month after your discharge from the program.

The first appointment, including this visit, may take up to an hour. However the anxiety questionnaire itself only takes 2 or 3 minutes to complete. The follow up monthly questionnaires will also be done at the same time you have a short clinical visit with the investigator. The final meeting to complete the last questionnaire will take place about a month after you leave treatment.

study completion, the information already collected may be used in the study, unless you request that the information be removed.

HIPPA: A separate consent form is attached which explains what HIPPA information will be used in this study.

Your signature below indicates your permission to take part in this research.

DO NOT SIGN THIS FORM AFTER THE IRB EXPIRATION DATE BELOW

Name of participant

Signature of participant | Date

Signature of person obtaining consent | Date

Printed name of person obtaining consent

My signature and date indicates that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the participant or the participant's legally authorized representative, and that informed consent was freely given by the participant or the legally authorized representative

Signature of witness to consent process | Date

Printed name of witness to consent process

VOID

Attachment 1

Research Consent Form Addendum: Authorization to Access Personal Health Information (PHI) under the Health Insurance Portability and Accountability Act (HIPPA).

Introduction
As part of your participation in the research study, 'Measuring Anxiety Post Detox in Residential Treatment', described in the attached consent form, the Principal Investigator, Janet Hutchison, MS, ARNP is seeking your permission to access personal health information (PHI) through which you can be identified, which is contained in your medical/clinical records at the Center for Drug-Free Living.

The PHI that we are requesting authorization to access is as follows: information about your medical or psychiatric diagnoses as well as medications you may be taking during the time that you are in this study.

All records containing your personal information, whether research or medical/clinical, will be kept secure and confidential. The attached consent form for the research study describes the confidentiality of your research records. This authorization form describes how PHI from your medical/clinical records, if needed, will be disclosed to the research team.

Purpose
This information will be used by the researcher to conduct the research study. The Principal Investigator will have access to your PHI for purposes of the study. Except as described in the consent form, no one else will have access to your PHI.

Additional Information

- This authorization will continue until the end of the research study. You may withdraw this authorization for the researcher to access and use your PHI at any time by contacting the Principal Investigator, in writing, at Janet Hutchison, The Center for Drug-Free Living, 100 West Columbia St, Orlando, FL 32806. If you withdraw your authorization the researchers may continue to use the information they have already collected. If you withdraw your authorization you will not be able to continue participation in the research.
- If you do not wish to authorize access to your PHI it will not be possible for you to participate in the study. It will not affect your continuing treatment at the Center for Drug-Free Living.
- Information provided to the research team will become part of the research records and will continue to be covered by the HIPAA Privacy Regulations while kept by the Center for Drug-Free Living. However, you should be aware that information disclosed by the research team to any other person or institution specified in the attached consent form may no longer be covered by the HIPAA Privacy Regulations.
- You will be given a signed copy of this authorization.

Signature and Authorization
I authorize the release of my medical/clinical records as described above.

_____ _____
Print Name Signature

Date: ___ ___ / ___ ___ / ___ ___ ___ ___

APPENDIX E: CITI TRAINING COMPLETION

COLLABORATIVE INSTITUTIONAL TRAINING INITIATIVE (CITI PROGRAM)

COURSEWORK TRANSCRIPT REPORT**

** NOTE: Scores on this Transcript Report reflect the most current quiz completions, including quizzes on optional (supplemental) elements of the course. See list below for details. See separate Requirements Report for the required scores at the time all requirements for the course were met.

- Name: Janet Hotaling (ID: 1305119)
- Email: [redacted]
- Institution Affiliation: University of Central Florida (ID: 405)
- Institution Unit: Nursing
- Phone: [redacted]

- Curriculum Group: Social and Behavioral Responsible Conduct of Research
- Course Learner Group: Same as Curriculum Group
- Stage: Stage 1 - RCR
- Description: This course is for investigators, staff and students with an interest or focus in Social and Behavioral research. This course contains text, embedded case studies AND quizzes.

- Report ID: 6625606
- Report Date: 01/01/2016
- Current Score**: 82

REQUIRED, ELECTIVE, AND SUPPLEMENTAL MODULES	MOST RECENT	SCORE
Mentoring (RCR-Interdisciplinary) (ID: 1250)	09/14/11	6/6 (100%)
Using Animal Subjects in Research (RCR-Basic) (ID: 13301)	09/17/11	5/8 (63%)
Research Involving Human Subjects (RCR-Basic) (ID: 13566)	09/17/11	10/11 (91%)
Introduction to the Responsible Conduct of Research Archived 1248 (ID: 1248)	09/17/11	No Quiz
Conflicts of Interest (RCR-SBE) (ID: 1462)	09/17/11	4/6 (67%)
Collaborative Research (RCR-SBE) (ID: 1484)	09/17/11	6/6 (100%)
Research Misconduct (RCR-SBE) (ID: 1495)	09/17/11	5/5 (100%)
Authorship (RCR-SBE) (ID: 1516)	09/14/11	4/5 (80%)
Peer Review (RCR-SBE) (ID: 1521)	09/14/11	3/5 (60%)
Data Management (RCR-SBE) (ID: 1523)	09/14/11	4/5 (80%)
Responsible Conduct of Research (RCR) Course Conclusion (ID: 1043)	09/17/11	No Quiz

For this Report to be valid, the learner identified above must have had a valid affiliation with the CITI Program subscribing institution identified above or have been a paid Independent Learner.

CITI Program
Email: citisupport@miami.edu
Phone: 305-243-7970
Web: https://www.citiprogram.org

COLLABORATIVE INSTITUTIONAL TRAINING INITIATIVE (CITI PROGRAM)

COURSEWORK REQUIREMENTS REPORT*

* NOTE: Scores on this Requirements Report reflect quiz completions at the time all requirements for the course were met. See list below for details. See separate Transcript Report for more recent quiz scores, including those on optional (supplemental) course elements.

- Name: Janet Hutchison (ID: 1305119)
- Email: [redacted]
- Institution Affiliation: University of Central Florida (ID: 405)
- Institution Unit: Nursing
- Phone: [redacted]

- Curriculum Group: Social and Behavioral Responsible Conduct of Research
- Course Learner Group: Same as Curriculum Group
- Stage: Stage 1 - RCR
- Description: This course is for investigators, staff and students with an interest or focus in Social and Behavioral research. This course contains text, embedded case studies AND quizzes.

- Report ID: 6625606
- Completion Date: 09/17/2011
- Expiration Date: N/A
- Minimum Passing: 80
- Reported Score*: 82

REQUIRED AND ELECTIVE MODULES ONLY	DATE COMPLETED	SCORE
Introduction to the Responsible Conduct of Research: Archived 1248 (ID: 1248)	09/17/11	No Quiz
Research Misconduct (RCR-SBE) (ID: 1495)	09/17/11	5/5 (100%)
Data Management (RCR-SBE) (ID: 1523)	09/14/11	4/5 (80%)
Authorship (RCR-SBE) (ID: 1518)	09/14/11	4/5 (80%)
Peer Review (RCR-SBE) (ID: 1521)	09/14/11	3/5 (60%)
Mentoring (RCR-Interdisciplinary) (ID: 1250)	09/14/11	6/6 (100%)
Using Animal Subjects in Research (RCR-Basic) (ID: 13301)	09/17/11	5/8 (63%)
Conflicts of Interest (RCR-SBE) (ID: 1462)	09/17/11	4/6 (67%)
Collaborative Research (RCR-SBE) (ID: 1484)	09/17/11	6/6 (100%)
Research Involving Human Subjects (RCR-Basic) (ID: 13566)	09/17/11	10/11 (91%)
Responsible Conduct of Research (RCR) Course Conclusion (ID: 1043)	09/17/11	No Quiz

For this Report to be valid, the learner identified above must has we had a valid affiliation with the CITI Program subscribing institution identified above or has we been a paid independent Learner.

CITI Program
Email: citisupport@miami.edu
Phone: 305-243-7970
Web: https://www.citiprogram.org

APPENDIX F: ZUNG SELF-RATING ANXIETY SCALE (SAS)

Zung Self-Rating Anxiety Scale (SAS)

For each item below, please place a check mark (9) in the column which best describes how often you felt or behaved this way during the past several days. Bring the completed form with you to the office for scoring and assessment during your office visit.

Place check mark (9) in correct column.	A little of the time	Some of the time	Good part of the time	Most of the time
1 I feel more nervous and anxious than usual.				
2 I feel afraid for no reason at all.				
3 I get upset easily or feel panicky.				
4 I feel like I'm falling apart and going to pieces.				
5 I feel that everything is all right and nothing bad will happen.				
6 My arms and legs shake and tremble.				
7 I am bothered by headaches neck and back pain.				
8 I feel weak and get tired easily.				
9 I feel calm and can sit still easily.				
10 I can feel my heart beating fast.				
11 I am bothered by dizzy spells.				
12 I have fainting spells or feel like it.				
13 I can breathe in and out easily.				
14 I get feelings of numbness and tingling in my fingers & toes.				
15 I am bothered by stomach aches or indigestion.				
16 I have to empty my bladder often.				
17 My hands are usually dry and warm.				
18 My face gets hot and blushes.				
19 I fall asleep easily and get a good night's rest.				
20 I have nightmares.				

Source: William W.K. Zung. A rating instrument for anxiety disorders. Psychosomatics. 1971

APPENDIX G: PTSD CHECKLIST – CIVILIAN VERSION (PCL-C)

PTSD CheckList – Civilian Version (PCL-C)

Client's Name: _____

Instruction to patient: Below is a list of problems and complaints that veterans sometimes have in response to stressful life experiences. Please read each one carefully, put an "X" in the box to indicate how much you have been bothered by that problem *in the last month*.

No.	Response	Not at all (1)	A little bit (2)	Moderately (3)	Quite a bit (4)	Extremely (5)
1.	Repeated, disturbing *memories, thoughts, or images* of a stressful experience from the past?					
2.	Repeated, disturbing *dreams* of a stressful experience from the past?					
3.	Suddenly *acting* or *feeling* as if a stressful experience *were happening* again (as if you were reliving it)?					
4.	Feeling *very upset* when *something reminded* you of a stressful experience from the past?					
5.	Having *physical reactions* (e.g., heart pounding, trouble breathing, or sweating) when *something reminded* you of a stressful experience from the past?					
6.	Avoid *thinking about* or *talking about* a stressful experience from the past or avoid *having feelings* related to it?					
7.	Avoid *activities* or *situations* because they *remind you* of a stressful experience from the past?					
8.	Trouble *remembering important parts* of a stressful experience from the past?					
9.	Loss of *interest in things that you used to enjoy?*					
10.	Feeling *distant* or *cut* off from other people?					
11.	Feeling *emotionally numb* or being unable to have loving feelings for those close to you?					
12.	Feeling as if your *future* will somehow be *cut short*?					
13.	Trouble *falling* or *staying asleep*?					
14.	Feeling *irritable* or having *angry outbursts*?					
15.	Having *difficulty concentrating*?					
16.	Being *"super alert"* or watchful on guard?					
17.	Feeling *jumpy* or easily startled?					

PCL-M for DSM-IV (11/1/94) Weathers, Litz, Huska, & Keane National Center for PTSD - Behavioral Science Division

PTSD CheckList – Civilian Version (PCL-C)

The PCL is a standardized self-report rating scale for PTSD comprising 17 items that correspond to the key symptoms of PTSD. Two versions of the PCL exist: 1) PCL-M is specific to PTSD caused by military experiences and 2) PCL-C is applied generally to any traumatic event.

The PCL can be easily modified to fit specific time frames or events. For example, instead of asking about "the past month," questions may ask about "the past week" or be modified to focus on events specific to a deployment.

How is the PCL completed?

- The PCL is self-administered
- Respondents indicate how much they have been bothered by a symptom over the past month using a 5-point (1–5) scale, circling their responses. Responses range from **1** *Not at All* – **5** *Extremely*

How is the PCL Scored?

1) Add up all items for a total severity score

or

2) Treat response categories **3–5** (*Moderately* or above) as symptomatic and responses **1–2** (below *Moderately*) as non-symptomatic, then use the following DSM criteria for a diagnosis:

- Symptomatic response to at least 1 "B" item (Questions 1–5),
- Symptomatic response to at least 3 "C" items (Questions 6–12), and
- Symptomatic response to at least 2 "D" items (Questions 13–17)

Are Results Valid and Reliable?

- Two studies of both Vietnam and Persian Gulf theater veterans show that the PCL is both valid and reliable (Additional references are available from the DHCC)

What Additional Follow-up is Available?

- All military health system beneficiaries with health concerns they believe are deployment-related are encouraged to seek medical care
- Patients should be asked, **"Is your health concern today related to a deployment?"** during all primary care visits.

• If the patient replies "**yes**," the provider should follow the Post-Deployment Health Clinical Practice Guideline (PDH-CPG) and supporting guidelines available through the DHCC and www.PDHealth.mil

APPENDIX H: PATIENT HEALTH QUESTIONNAIRE (PHQ-9)

PATIENT HEALTH QUESTIONNAIRE (PHQ-9)

NAME:_____ DATE:_____

Over the last *2 weeks,* how often have you been bothered by any of the following problems?
(use "✓" to indicate your answer)

	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself—or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed. Or the opposite — being so figety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead, or of hurting yourself	0	1	2	3
		add columns	+	+

(Healthcare professional: For interpretation of TOTAL, please refer to accompanying scoring card). TOTAL:

10. If you checked off *any problems,* how *difficult* have these problems made it for you to do your work, take care of things at home, or get along with other people?

- Not difficult at all _____
- Somewhat difficult _____
- Very difficult _____
- Extremely difficult _____

A2663B 10-04-2005

PHQ-9 Patient Depression Questionnaire

For initial diagnosis:

1. Patient completes PHQ-9 Quick Depression Assessment.
2. If there are at least 4 ✓s in the shaded section (including Questions #1 and #2), consider a depressive disorder. Add score to determine severity.

Consider Major Depressive Disorder

- if there are at least 5 ✓s in the shaded section (one of which corresponds to Question #1 or #2)

Consider Other Depressive Disorder

- if there are 2-4 ✓s in the shaded section (one of which corresponds to Question #1 or #2)

Note: Since the questionnaire relies on patient self-report, all responses should be verified by the clinician, and a definitive diagnosis is made on clinical grounds taking into account how well the patient understood the questionnaire, as well as other relevant information from the patient.
Diagnoses of Major Depressive Disorder or Other Depressive Disorder also require impairment of social, occupational, or other important areas of functioning (Question #10) and ruling out normal bereavement, a history of a Manic Episode (Bipolar Disorder), and a physical disorder, medication, or other drug as the biological cause of the depressive symptoms.

To monitor severity over time for newly diagnosed patients or patients in current treatment for depression:

1. Patients may complete questionnaires at baseline and at regular intervals (eg, every 2 weeks) at home and bring them in at their next appointment for scoring or they may complete the questionnaire during each scheduled appointment.
2. Add up ✓s by column. For every ✓: Several days = 1 More than half the days = 2 Nearly every day = 3
3. Add together column scores to get a TOTAL score.
4. Refer to the accompanying **PHQ-9 Scoring Box** to interpret the TOTAL score.
5. Results may be included in patient files to assist you in setting up a treatment goal, determining degree of response, as well as guiding treatment intervention.

Scoring: add up all checked boxes on PHQ-9

For every ✓ Not at all = 0; Several days = 1;
More than half the days = 2; Nearly every day = 3

Interpretation of Total Score

Total Score	Depression Severity
1-4	Minimal depression
5-9	Mild depression
10-14	Moderate depression
15-19	Moderately severe depression
20-27	Severe depression

A2662B 10-04-2005

APPENDIX I: SELF-ADMINISTERED STATE-TRAIT ANXIETY INVENTORY (STAI-6)

Self-Administered State-Trait Anxiety Inventory (STAI-6)*

Study Number _____ Date _____

A number of statements that people have used to describe themselves are given below. Read each statement and then circle the most appropriate number to the right of the statement to indicate how you feel *right now, at this moment.* There are no right or wrong answers. Do not spend too much time on any one statement but give the answer that seems to describe your present feelings best.

	Not at all	Somewhat	Moderately	Very much
1. I feel calm	1	2	3	4
2. I am tense	1	2	3	4
3. I feel upset	1	2	3	4
4. I am relaxed	1	2	3	4
5. I feel content	1	2	3	4
6. I am worried	1	2	3	4

Please make sure that you have answered *all* the questions.

Note. * Adapted from "The development of a six-item short-form of the state scale of the Spielberger State-Trait Anxiety Inventory (STAI)," by T. M. Marteau and H. Bekker, 1992, *British Journal of Clinical Psychology, 31,* p. 306. Copyright 1992 by the British Psychological Society. Reprinted with permission.

APPENDIX J: JANET HUTCHISON ACADEMIC CV 2016

Janet Mary Hutchison, MS, ARNP,
1700 Lake Shore Drive
Orlando, Florida, 32803
Phone: 407-257-9238
Email: jhutchi890@aol.com
Florida License: ARNP 3236322

ACADEMIC DEGREES

PhD Student - University of Central Florida 2007 – current – Nursing
Dissertation Completed, to defend Spring 2016

Post Masters Certificate – Drexel University 2015 - Psychiatric Mental Health Nurse Practitioner

MS – University of Texas, San Antonio 1981 – Adult Nurse Practitioner
Thesis: Personality Characteristics of Army Nurse Practitioners.

BSN – University of Maryland (WRAIN), 1973 – Nursing

ACADEMIC POSITIONS

2016 Clinical Preceptor. Psychiatric Mental Health Nurse Practitioner Student.. University of South Alabama

2013 Clinical Preceptor. Duke University PA program.

2007-2008 Clinical Preceptor, Psychiatric Nurse Practitioner Students, University of South Florida

2005–2008 Clinical Mentor, Florida Hospital Osteopathic Family Practice Residency

1997-1999 Adjunct Instructor, Orlando Vocational Technical Institute, Orlando, Fl. CNA course for High School Students
Medical Careers Course – Dr Phillips High School

1994-1996 Adjunct Instructor, University of Texas School of Nursing, El Paso, Texas
Physical Assessment for 3rd year Nursing Students
GYN exams and clinical supervision Nurse Practitioner program

1981-1982 Adjunct Instructor, City College of Chicago in Brunsum, Netherlands
EMT-A

PROFESSIONAL EXPERIENCE/CLINICAL PRACTICE

2012- Present Nurse Practitioner, Orange Blossom Family Health Center. Provide community mental health services to an underserved adult population. Practice includes Initial Psychiatric Evaluations, medication management and brief psychotherapy.

2010- 2015 Nurse Practitioner, Center for Drug Free Living/Aspire Health Partners, Orlando, Florida. 32806 I returned to my prior position in clinical care at the Center for Drug Free Living after completing my military recall.

2008-2010 Commander, 212th Med Detachment (CSC), FOB Diamondback (Iraq). APO AE, 09334. Returned to Active Duty as a retiree recall, I prepared and deployed a Combat Stress Control Unit consisting of 45 Behavioral Health Officers and Technicians to Northern Iraq.

2002-2008 Nurse Practitioner, Center for Drug Free Living, Orlando, Florida 32806 Practice included; Initial assessment, continued medical and/or psychiatric management and detoxification of addicted patients presenting to a 44 bed inpatient detoxification facility, medical management of primary care and mental health problems for adults and adolescents in substance abuse residential treatment; Initial assessment and treatment of substance abusing adults in outpatient services referred for treatment with methadone or suboxone, or other medical protocols used in recovery.

1998-2002 Nurse Practitioner/Manager, Health Care Center for the Homeless, Orlando, Fl. Provided primary care and chronic disease follow-up to a wide variety of homeless individuals. I developed a quality assurance program and operational procedures for the clinic to include job descriptions for all personnel. I wrote the initial proposal for subsequent funding as a Health Care for the Homeless clinic.

1993-1996 Nurse Practitioner, Planned Parenthood, El Paso, Texas. I provided primary care in women's health to clients ranging in age from adolescence to old age.

1973-1990 Army Nurse Corps Officer, US Army. Various assignments around the world in both clinical and administrative positions: generally in outpatient or emergency room settings.

CERTIFICATIONS

Basic Life Support	Current
Advanced Cardiac Life Support	Current
Adult Nurse Practitioner (ANCC)	Current
Addictions – Advanced Practice (ANCB)	Current
Psychiatry Mental health Nurse Practitioner (ANCC)	Current

AWARDS AND SCHOLARSHIPS

2012 IntNSA - Research Scholarship -$2000- for dissertation research

PUBLICATIONS

2015 Norris, A., Pettigrew, J., Day-Miller, M., Hecht, J., Hutchison, J., & Campoe, C. (2015). Resisting pressure from peers to engage in sexual behavior: What communication strategies do early adolescent latino girls use? *Journal of early adolescence*. 35(4). 562-580. Doi: 10.1177/0272431614544962

PRESENTATIONS

Hutchison, J.M. (2012). Anxiety in substance abuse treatment and relationship to early relapse. Paper presented at the Center for Drug Free Living, Orlando, Fl. September

Hutchison, J.M. (2012). Measuring intentions to resist peer pressure. Paper presented at the annual meeting of the Southern Nursing Research Society. New Orleans LA, Feb. 25

Hutchison, J.M. (2005). Short detoxification for opiate dependent patients using buprenorphine. Poster presented at the annual meeting of the Health Care for the Homeless National Conference, Washington DC, June.

PROFESSIONAL AFFILIATIONS

International Nurses Society on Addictions	2008- Present
Central Florida Nurse Practitioner Counsel	1998 - Present
American Nurses Association	1997 – Present
Florida Nurse Association	1997 – Present