The Effect of Cranial Electrotherapy Stimulation (CES) on Anxiety Symptoms Following Opiate and Alcohol Withdrawal - An RCT

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Objectives

1) Identify and discuss the rationale for this study.
2) Focus on effect of anxiety on learning and effect of current pharmaceuticals used to treat anxiety on sedation.
3) Discuss this study development and data collection to include the effect of cortisol on anxiety and substance abuse
4) Discuss the study results and what could have been done differently
5) Identify lessons learned and applications to practice.

Why Anxiety?

- Most common co-occurring disorder associated with substance abuse
- Prominent negative emotion following detox
- Limited data on anxiety measurement during the first month in recovery

Scope of the Problem

- Anxiety and associated stress are often cited as reasons for early treatment dropout (Levy, 2008, McGuinness, & Fogger, 2006)
- More than 50% of patients experience heightened anxiety symptoms immediately following detox from alcohol or opiates
- Greater than 25% of these patients will drop out of residential treatment within the first 30 days
- Of the patients with anxiety, who complete treatment, only 40% were abstinent at 6 months (Daughters, Lejuez, Kahler, Strong, & Brown, 2005)

Theoretical Basis

The **self-medication hypothesis** (Khantzian & Albanese,2008) proposes that substance abuse is an individuals effort to calm emotional dysregulation associated with anxiety

Self-medication hypothesis

- Approximately 25% of people in the US will be diagnosed with an anxiety disorder during their life. Often this diagnosis is made prior to age 18 (Kessler et al, 2005)
- More than 50% of individuals with a substance use disorder feel they had preexisting anxiety symptoms prior to their substance abuse (Scott & Hulvershorn, 2011)

Theoretical Basis

The **Theory of 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).

Theory of Allostasis

- 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** (high allostatic load) and is a response to fear.

Effect of Anxiety on Substance Abuse Treatment and Early Relapse in Residential Substance Abuse Treatment

Anxiety Study – Sample

This was a prospective study 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 days and 60 days

Aims of the Study

- Do patients who fail to complete residential treatment differ in level of anxiety symptoms on admission from those who complete treatment?
- Do patients who relapse, or leave residential treatment prior to completion, have higher anxiety scores prior to discharge than individuals who complete treatment?
- Do self-report of PTSD symptoms affects change in anxiety symptoms during the first 60 days of substance abuse recovery? (PTSD measured using the PCL-C)
- Is reported PTSD a significant factor in drop-out from residential treatment prior to completion?

Results of (prospective) Anxiety Study

1.) The relationship between Zung anxiety scores on admission and leaving treatment early were not significant (p-value =.96)

2.) There was a significant difference between the last measured anxiety score and leaving treatment prior to completion (p-value < .02) when compared to treatment completers.

3.) 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-value >.08).

4.) Men with PTSD did not leave treatment prior to completion more frequently than those without PTSD.

State of the Science

Use of Complementary and Alternative therapies (CAM) in the treatment of anxiety in substance abuse recovery

- Relapse rates remain high in early treatment
- Sustained recovery is less than 50%
- Medications can cause over sedation and decreased ability to learn recovery techniques

State of the Science – Use of CAM

- Acupuncture, massage therapy, yoga, meditation, exercise and music have often integrated into substance abuse treatment
- There is also a renewed interest in manipulating neuron response through the use of low level electrical or magnetic currents through modalities such as:
  - Electro Convulsive Therapy (ECT);
  - Deep Brain Stimulation (DBS);
  - Transcranial Magnetic Stimulation (TMS);
  - Trans cranial Direct Current Stimulation (tDCS) and
  - Cranial Electrotherapy Stimulation (CES).

State of the Science – Use of CAM

- The most promising modality appeared to me to be CES: This modality did not require individual monitoring or specialized group attendance, and if effective could be used by the individual on an ongoing basis, and therefore may hold promise for enhancing long term recovery.

Effect of Cranial Electrotherapy Stimulation (CES) as a Method to Decrease Anxiety Symptoms Following Opiate and Alcohol Withdrawal

CES Study – Parameters

- This was a double blind experimental study using repeated measures and two treatment conditions (intervention/active and control/placebo).
- The intervention was conducted over a period of 15 days during the first 3 weeks following medical detox from opiate/alcohol.

Aims of the CES Study

- Compare in men in early substance recovery treatment for substance abuse the effects of Cranial Electrotherapy Stimulation or placebo on anxiety and depression.
- Compare in men in early substance recovery treatment for substance abuse the effects of Cranial Electrotherapy Stimulation or placebo on cortisol level.

CES Study – Setting

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 included daily group sessions with psychoeducation as well as weekly individual counseling. In this environment, participants could be monitored for compliance with the treatment protocol.

CES Study – Sample

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:

- Having an implantable electrical device (this exclusion criterion was recommended by the CES manufacturer);
- Unable to read or understand English and;
- Recent dental surgery or bleeding oral lesions (blood in the salivary cortisol specimen affects accuracy of measurement).

CES Study – Methods

Demographic data, Zung SAS and PCL-C were collected when participant was enrolled in the study on arrival at the residential program

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, then they were withdrawn from the study.

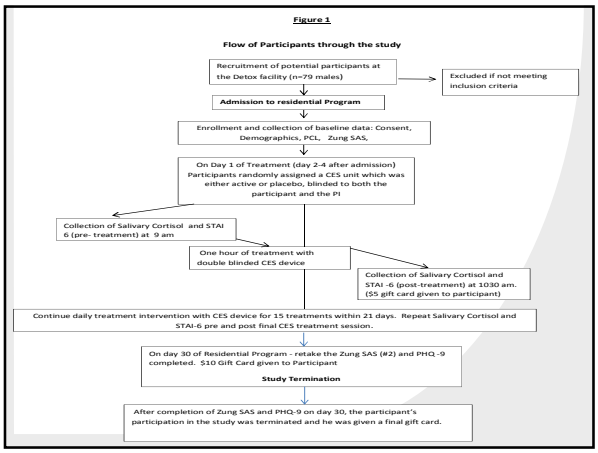
CES Study – Methods

- 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.
  - Between 8:15 a.m. and 8:45 a.m. and again
  - Between 9:30 and 10:00 a.m. following completion of the hour long treatment on these days.
- Since morning cortisol levels usually peak within 2 hours of arising and then gradually decrease during the day, collection these time points allowed for consistency between participants.
- State anxiety, using the STAI 6 was collected at these same 4 time points.

CES Study – Methods

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 also measured at study enrollment.

Depression, using the PHQ-9, was measured at 30 days as recommended in the literature (Hepner, et al 2009).



CES Study – Sample Characteristics

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%)

CES Results – Anxiety & 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

CES Results – 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

CES Results – 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.
- 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.

CES Study – Implications for Treatment

- 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 may behave differently and perhaps should be studied separately.
- The cultural and social differences in these populations may also affect outcomes.

CES Study – Implications for Treatment

- 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.
- 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 benefit from prolonged use.

CES Study – Strength & 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.

CES Study – 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, and there was trending towards improvement of symptoms in the CES group.

CES Study – Conclusion

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.

CES Study – Conclusion

An additional study measuring cortisol and anxiety in a control group of substance abusing men who have completed detox and were awaiting residential placement and also with 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 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.

CES Study – Conclusion

In a future study, multiple arms in a trial, such as treatment, placebo and control group, might result in statistically significant outcomes.

Questions? Comments?

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