

CES in the Treatment of Addictions: A Review and Meta-Analysis

Addictions are serious and poorly understood problems that may involve prescribed or illicit drugs, alcohol, or compulsive behavioral patterns involving sex, gambling, eating or “surfing the net.” Cranial electrotherapy stimulation (CES) has been shown in 15 studies to quickly, safely and effectively reduce the physical withdrawal, psychological cravings and co-morbid anxiety, insomnia and depression in people suffering from addictive disorders.

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For decades, our national anti-drug motto was “Just Say No!” It has never served as anything other than a catchy public relations phrase. In fact, the motto itself became an instant hit among the purveyors of illicit substances during decades of anti-establishment activities. The motto has also been

a grim disguise for many years of chronic human destructiveness involving both legal and illegal substances, and has even been a political invective foisted against various candidates for political office. Agencies for detoxification, “rehabilitation,” and other types of addiction treatment tried unsuccessfully to replace “just say no” with “just say yes” to positive lifestyle alternatives, but it never worked unless the treatment program itself was powerful and had very long-term follow-up.

Volumes have been written about addiction and billions of dollars have been spent on the problem. But the definition of addiction is far from clear. Not understanding a complex addiction problem often results in unnecessary hospitalization, increased medical costs, and patients who develop a distrust of both healthcare practitioners and “rehabilitation” organizations. Conversely, without a universally-accepted definition of addiction, many people on destructive life paths fail to receive the care they require. Nevertheless, realistic practice guidelines for the addictions are either unavailable or equivocal. This produces difficulties with both patient management and reimbursement.

Addictive behaviors present confusing and complex patterns of human activity.¹ While most people think of alcohol and other drug (substance) dependence as the primary addictions, these addictions are definitely surpassed in number by dependence upon excessive sugar, caffeine, and nicotine. It has also been said that eating disorders, compulsive gambling, excessive sexual behavior, and other intemperate behavior patterns might also be considered as behavioral dependencies or addictions. While prevalent in many cultures, such behaviors have historically defied explanation. Nevertheless, these behavioral dependencies often also have specially-designed supportive programs that incorporate a 12-Step Program similar to what has been a *sine qua*

non of effective treatment programs that focus on alcoholism and the abuse of other substances. Just as there is an Alcoholics Anonymous, there are also groups such as Gamblers Anonymous and Overeaters Anonymous. The American Psychiatric Association considers a diagnosis of Pathological Gambling to be a form of “Impulse-Control Disorders Not Elsewhere Classified” in the DSM-IV-TR.²

The DSM-IV-TR also divides substance-related disorders into two broad categories, Substance Use Disorders and Substance-Induced Disorders (see Table 1).

From a psychiatric point of view, Table 1 illustrates the broad complexity and the wide-ranging, protean manifestations of addiction. Addiction can occur as part of many different psychiatric disorders, but can also induce them as the Table indicates. Addiction does not usually just happen, “out of the blue.” There is a progression through use, habituation, abuse, dependence, intoxication, and withdrawal. Individual vulnerabilities interact with various psychopharmacologic facets of one or more substances to produce both immediate and, occasionally, persistent

TABLE 1. CATEGORIES OF DSM-IV-TR SUBSTANCE RELATED DISORDERS²

Substance Use Disorders

- Substance Dependence
- Substance Abuse

Substance-Induced Disorders

- Substance Intoxication
- Substance Withdrawal
- Substance-Induced Delirium
- Substance-Induced Persisting Dementia
- Substance-Induced Persisting Amnesic Disorder
- Substance-Induced Psychotic Disorder
- Substance-Induced Mood Disorder
- Substance-Induced Anxiety Disorder
- Substance-Induced Sexual Dysfunction
- Substance-Induced Sleep Disorder

and long-term destructive effects. The DSM-IV-TR groups all substances into 11 classes and gives detailed criteria sets of Intoxication and Withdrawal for each substance class. The main DSM-IV-TR classes of substances of abuse are listed in Table 2.

DSM-IV-TR actually lists two other classes of substances, which are labeled as "Polysubstance" and "Other." Clinically-active professionals from any discipline will understand the importance of these two additional categories. Polysubstance abuse often presents the most puzzling and challenging sets of symptoms that can appear completely refractory to treatment when the multiple substances are not recognized or admitted by history. The "other" category gives not so silent testimony to the waves of newer designer drugs and novel but dangerous homemade combinations of substances that may be relatively innocuous and readily available over the counter in most drug stores and pharmacies. In the year 2007, Western ingenuity has produced a frequently deadly combination of heroin and Tylenol® P.M. known as "cheese." This finely ground up powder can be sold inexpensively and snorted (inhaled) or injected.

Despite the apparently robust medical nosology of addiction, there is an uncomfortable gap between the medical certainty of naming and classifying addictions and the vexatious problems of devising most effective treatment methodologies. There is such distance between the theory and clinical practice of dealing with addiction that many successful long-term programs have minimal medical input only during the acute phase of withdrawal and focus instead on the psychosocial aspects. Ideally, adequate therapeutics focus on both medical and psychosocial aspects, as well as providing long-term follow-up.

A substantial number of "rehab" programs are administered by recovered addicts and eschew medical input, except for emergencies. One value of these "indigenous" rehab programs is that they illustrate the spectrum of ideas about addiction. Very robust non-medical components of modern addiction treatment often highlight the element of self-help. In the 21st century, self-help almost universally includes the processing of both reliable and unreliable internet-based information. A search of the web provides a va-

riety of definitions for addiction, and reveals the diversity of thinking about addictions:

1. Inconsistent use of terms such as addiction, dependence and tolerance, often results in misunderstandings between regulators, health care providers, patients and the general public regarding the use of medications for the treatment of pain. Because of these misunderstandings, pain is often under-treated and individuals may be stigmatized because of their use of opioids for medical purposes.³

2. Addiction is a term referring to compulsive drug use, psychological dependence, and continuing use despite harm. Addiction is frequently and incorrectly equated with physical dependence and withdrawal. Physical dependence, not addiction, is an expected result of opioid use.⁴

3. Addiction is a chronic, relapsing disease, characterized by compulsive drug-seeking and drug use, as well as by neurochemical and molecular changes in the brain.⁵

4. Dependence on a substance (such as alcohol or other drugs) or an activity, to the point that stopping is very difficult and causes severe physical and mental reactions may also be considered addiction.⁶

5. A compulsive physiological craving for a habit-forming substance, addiction is a chronic and progressive disease usually characterized by physiological symptoms upon withdrawal. The term "dependence" is often used synonymously to avoid the pejorative connotations of addiction.⁷

6. Addiction can also be strong emotional and/or psychological dependence on a substance such as alcohol or drugs that has progressed beyond voluntary control.⁸

7. Psychological dependence occurs when the user experiences an overwhelming desire to continue with the drug experience. This can be because of the pleasurable effects and the desire to keep experiencing them. It can, however, also represent a form of "psychological crutch." The drug experience can become a way of blocking out reality, making life bearable, and a way of facing the world. Without this crutch, life seems worthless. It can happen with any drug or any activity which takes over a person's life including eating, sex, work, or jogging.⁹

8. An addiction is a recurring compulsion by an individual to engage in some

TABLE 2. MAIN CLASS DIVISIONS FOR SUBSTANCES OF ABUSE THAT ARE RECOGNIZED BY DSM-IV-TR

- Alcohol
- Amphetamines
- Caffeine
- Cannabis
- Cocaine
- Hallucinogens
- Inhalants
- Nicotine
- Opioids
- Phencyclidine
- Sedatives, hypnotics, or anxiolytics

specific activity. The term is often reserved for drug addictions but it is sometimes applied to other compulsions, such as problem gambling, compulsive overeating, and hyperreligiosity.¹⁰

9. It can be important to provide a definition of what addiction is not. Addiction has nothing to do with either lack of willpower or intelligence. People with addiction problems often are above-average in both categories. For many, their habit started as a way of coping with unbearable feelings they couldn't deal with in any other way. Through a mixture, perhaps, of life experiences, social pressures and genetic inheritance, addicted individuals have lost control over their behavior; their drinking or their drug-taking, and suffer cravings or withdrawal symptoms if they go without.¹¹

10. An addiction is any behavior that is repeated despite negative consequences. A behavior becomes addictive when it permanently alters moods or emotions.¹²

One website even recognizes compulsive internet searching as an addiction. The Center for Online Addiction offers hope and valuable resources to those seeking information about Internet addiction. Internet addiction is a type of compulsive disorder...a new form of addictive behavior.¹³ This definition alludes to the degrees of desocialization and maladaptive interpersonal processes found in many addicts. Nonetheless, we will probably soon be recognizing that much of the computer experience has some positive neurocognitive effects including more sophisticated eye-hand coordination, enhanced abilities to concentrate and multi-task, and novel abilities to learn, grow, and socialize in different forms of immersive virtu-

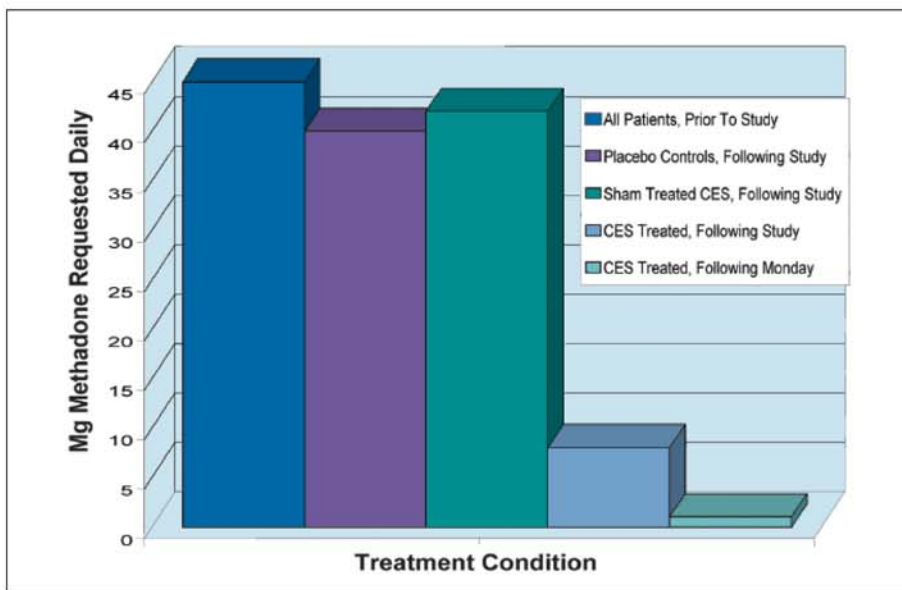


FIGURE 1. CES Methadone Self Withdrawal Study. This graph shows near elimination of the need for methadone over a two week period in the CES treated group, but not in the two control groups.

al reality (IVR).

Neuroadaptation, a phenomenon seen in tolerance (tachyphylaxis), habituation and withdrawal, may result during the course of repetitive behaviors. Neuroadaptation reflects the brain's ability to adjust to any stimulus or influence which affects the brain's normal functioning. Although the term is used frequently in discussion of problems with chemicals and drugs, even some modes of purely electrical stimulation such as neural stimulators can be affected by neuroadaptation. However, neuroadaptation is not the same as addiction. Many people who use narcotics for chronic pain syndromes never display addictive behaviors even though they have become physically dependent on psychoactive substances. Curtailing or eliminating substance use does not necessarily end addiction, since addictive behavior patterns such as gambling exist in the absence of substance abuse.

Psychoactive drugs and certain other activities influence both experience and neurochemistry in positive as well as negative directions. This can include activities such as gambling, aerobic exercises, surfing the web, and meditating. Just as the use of exogenous substances produces "imposter" transmitter molecules vying for receptor sites within the brain, various repetitive activities are also capable of stimulating naturally occurring neurotransmitters.¹⁴⁻¹⁶ The relationship between the addicted person and the object of their excessive, often obsessive behavior

indicates that it is the confluence of psychological, social and biological forces that determines addiction. No single set of factors adequately explains the multifactorial causes.^{1,17}

Addiction Research with CES

The *Arndt-Schultz Law* states that a small stimulus will provoke the body positively, while a larger signal has no further effect, and a very large signal actually has a suppressive effect in the opposite of the desired direction.¹⁸ In an early study of CES treatment for alcoholism, it was decided to seek an answer to the age old question, "if a little is good, might more be even better?" Three hundred alcoholic patients were selected. One hundred patients received a sub-therapeutic dose of only 20 microamperes of CES current, while the second hundred were allowed to turn the current up to a level that felt comfortable and maintain it at that level. In the third group of 100 patients, the current was turned up to their maximum comfortable tolerance. The group receiving only 20 microamperes did not experience any clinical change, while the group getting too much current also did not change and some of their scores actually tended to worsen. The group treated at their self perceived comfort level was the only group to experience significantly effective results from CES treatment.¹⁹ Today CES is applied by turning up the current until slight vertigo is experienced, then lowering the current until the vertigo complete-

ly disappears and the current is at a comfortable level. In CES treatments, more is not better, so there is never a need to endure an uncomfortably high current.

In 1959, Obrosow warned that the patient must be placed in a dark, quiet room in a reclining position if electrosleep (a name formally used for CES therapy) was to be successful.²⁰ It is now known that people can go about their business while they do a CES treatment and not lose any effect. People in shopping malls can be seen wearing their CES device, as can executives at their desk, or patients during cognitive psychotherapy. It is, of course, inadvisable to drive or operate heavy machinery as vertigo is a common side effect during treatment and, in rare cases of patients with a history of vertigo, it may persist for hours or days before wearing off.

It is also now known that CES can function as an electrophysiologic equivalent of deep muscular relaxation, which means that the patient who decides to sit or lie still during a CES treatment while focusing on slow, deep abdominal breathing may reap a clinical bonus similar to what is observed with a self-directed meditation practice.

Some CES addiction research was discussed in our previous *Practical Pain Management* series of articles on anxiety and depression. This is mentioned because addiction can produce anxiety and depression as well as the full spectrum of "autonomic (sympathetic) overflow."

CES may produce its effect on addiction with ear-clip electrodes through achieving parasympathetic nervous system dominance by stimulating the auricular branch of the vagus nerve. Withdrawal symptoms are basically manifestations of sympathetic nervous system overflow or overactivity (e.g., tremors, sweating, tearing, etc.) Parenthetically, this may also explain the observed efficacy of CES in treating some patients with reflex sympathetic dystrophy.²¹

In one single-blind CES study of methadone detoxification, 28 male heroin addicts between the ages of 18 and 60 were selected on the basis of having severe anxiety as measured by the Hamilton Anxiety Scale (HAS) and Taylor Manifest Anxiety Scale (TMAS).²² They also reported difficulties in sleeping, and expressed a willingness to participate in the study for at least two weeks while on a locked hospital ward. Patients in this study also agreed not to take any tranquilizers

or hypnotics while in the study. This was a self-medicated withdrawal study in which methadone was given as requested by the patients as needed to control their withdrawal symptoms. The patients were then randomly divided into a CES treatment group (N=14) who were taking 20-60mg of methadone/day, a sham CES group (N=7) taking 30 to 40mg methadone/day, and a "waiting list" placebo control group (N=7) taking 25-40mg methadone/day but receiving neither CES nor sham CES.

CES or sham CES were given for ten days, Monday through Friday, 30 minutes per day. After six to eight CES treatments (see Figure 1), methadone intake was zero in nine patients, with another patient achieving zero methadone intake after ten treatments. Three other patients were taking 10-15mg of methadone daily after the ten treatments. One other patient in the active CES group dropped out of the study after the first treatment. All patients treated with active CES reported feeling restful and having a general feeling of well-being during the study, and their sleep was good and undisturbed after three treatments. The TMAS scores came down significantly in the CES group, as seven patients dropped from a mean of 31 before CES to a mean score of 20 after ten days of the treatment (normal TMAS score is 8-18). The other CES treated patients showed a 25 - 50% reduction in their TMAS scores.

Sham CES patients showed an insignificant change in the mean TMAS scores that ranged from 29 to 27. The methadone intake did not change in four sham CES patients, and only dropped 5-10mg in the other three sham CES patients. These patients receiving sham CES were anxious and depressed, and complained of both difficulty sleeping and other somatic problems. The seven control patients also did not do well, TMAS scores increased in two control patients, was the same in one, and only decreased one to two points after ten days in the remaining patients.

Methadone intake was the same in three control patients, and decreased in the other four control patients after ten days. These patients were anxious and had difficulty sleeping. HAS scores were also diminished in the CES group but not in the two control groups.

In a CES study of cocaine addicts, 25 consecutive patients who met criteria for

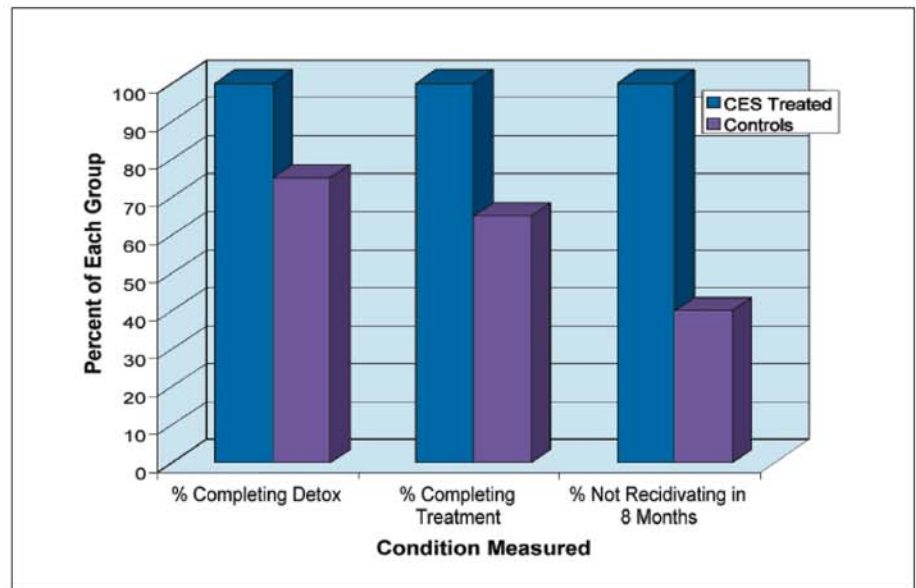


FIGURE 2. CES Cocaine Addiction Study. This graph shows 100% of the CES treated group, but not the control group, completed treatment and avoided recidivism.

a DSM III diagnosis of cocaine abuse were admitted to a drug abuse treatment hospital in Los Angeles (See Figure 2).²³ Patients were alternately assigned to a control group (N=12), and Alpha-Stim CES treatment (N=13). Of the patients assigned to the treatment group, only five accepted CES treatment while eight refused CES treatment. CES was given for 20 minutes twice a day for the five-day inpatient treatment program. All five (100%) of the CES patients completed detoxification while 75% of the other 20 patients did not. All five (100%) of the CES patients completed the treatment program, compared with 63% of the CES refusers and 67% of the other twelve controls who did not complete the treatment program. Follow-up on all patients—6 to 8 months later—showed that no CES patients had returned for treatment while 50% of the CES refusers and 39% of the controls had relapsed. One of the control patients had died of an overdose.

The role of CES in the treatment of chemical dependency is of great interest since anxiety and insomnia are frequently present in the early stages of recovery and these symptoms are a common precursor to relapse. The authors concluded that CES facilitated patient retention in a hospital detoxification and rehabilitation program for cocaine dependent persons.

Table 3 details 15 studies out of more than 25 studies in the literature that utilized one form or another of electrical stimulation to the head on either humans

or animals. As with all competent research, these studies were conducted only after careful planning. Rigorous research is usually preceded by a pilot study to ensure obtaining a measurable treatment effect before launching a larger, relatively expensive, and time consuming study. In other instances, such as the study of P300-evoked potential change in polysubstance abuse, clinicians sometimes observe the same or similar change happening every time they give a specific type of treatment. Therefore, such clinical observations become the basis from which to launch a larger study. Studies that treated rodents with auricular electro-acupuncture on the ear lobes to assess the changes it made in the serum endorphins are not listed.^{24,25} Other studies that are not shown sought to elucidate the levels of endorphins, or the metabolism of biogenic amines in alcoholic addicts.²⁶⁻²⁸

As explained in detail in our previous articles on anxiety and depression in this journal, all scores within each study were converted to Zr scores and then the average Zr score was taken from each study.^{41,42} This yielded one Zr score per study, which was then weighted by the number of subjects in the study. The average n weighted Zr score was then converted to an r effect size of $r = .65 \pm .08$, with a confidence interval of .42 to .88. In this analysis, the r effect size is a direct measure of the combined percent effectiveness of CES treatment found in these investigations, regardless of what each study was analyzing;

TABLE 3. META-ANALYSIS OF CES ADDICTION STUDIES

| Author | Addiction Studied | Treated | Control | Study Design | Vector Measured | Instrument | Improvement | Zr Score |
|--------------------------|-------------------|---------|---------|---------------|---|---------------------------|-------------|---------------|
| Bianco ²⁹ | Polysubstance | 11 | 9 | Double Blind | Anxiety | Hamilton | 71% | .887 |
| | | | | | Anxiety | Beck | 77% | 1.020 |
| | | | | | Depression | Hamilton | 78% | 1.045 |
| | | | | | Depression | Beck | 76% | .996 |
| Boertien ³⁰ | Smoking | 20 | | Open Clinical | Reduced Smoking | Self Report | 65% | .775 |
| Braverman ³¹ | Polysubstance | 13 | 2 | Open Clinical | P300 evoked Potential | BEAM EEG | p.05 | .549 |
| Gomez ²² | Methadone | 14 | 14 | Double Blind | Methadone Reduction Anxiety | Treatment Records IMAS | 93% 38% | 1.658 .400 |
| Brovar ²³ | Cocaine | 5 | 12 | Double Blind | % completed Detox, more than controls | Treatment Records | 25% | .255 |
| | | | | | % completed Program, more than controls | Treatment Records | 37% | .388 |
| | | | | | % Recidivating, 8 mos., less than controls | Treatment Records | 50% | .549 |
| Krupitsky ³² | Alcohol | 10 | 10 | Double Blind | State Anxiety | STAI | 23% | .234 |
| | | | | | Trait Anxiety | STAI | 73% | .929 |
| | | | | | Anxiety | TMAS | 48% | .523 |
| | | | | | Depression | Zung | 23% | .234 |
| | | | | | Depression | MMPI | 30% | .310 |
| | | | | | MAO-B | Serum | 32% | .332 |
| | | | | | β-endorphin | Serum | 33% | .343 |
| McKenzie ³³ | Alcohol | 10 | 10 | Double Blind | Anxiety | CAQ | 60% | .693 |
| | | | | | Depression | CAQ | 34% | .354 |
| | | | | | Sleep | SRS | 16% | .161 |
| Overcash ³⁴ | Marijuana | 16 | 16 | Open Clinical | Stress | EMG | 95% | 1.832 |
| | | | | | Anxiety | 16PF | 80% | 1.099 |
| | | | | | Assertiveness | 16PF | 55% | .618 |
| | | | | | Ego Strength | 16PF | 61% | .709 |
| Schmitt ³⁵ | Polysubstance | 26 | 23 | Double Blind | Digit Symbol | WAIS | 62% | .725 |
| | | | | | Digit Span | WAIS | 49% | .536 |
| | | | | | Object Assembly | WAIS | 74% | .950 |
| | | | | | Full Scale I.Q. | WAIS | 72% | .908 |
| Schmitt ³⁶ | Polysubstance | 30 | 30 | Double Blind | Anxiety | IPAT | 43% | .460 |
| | | | | | State Anxiety | STAI | 63% | .741 |
| | | | | | Trait Anxiety | STAI | 67% | .811 |
| Smith ³⁷ | Alcohol | 45 | 40 | Double Blind | Mazes | Rev Beta | 34% | .354 |
| | | | | | Form Board | Rev Beta | 35% | .365 |
| Smith ³⁸ | Alcohol | 53 | | Open Clinical | Withdrawal Tremor | Tremor Meter | 59% | .678 |
| Smith ¹⁹ | Alcohol | 24 | 23 | Double Blind | Anxiety | POMS | 50% | .549 |
| | | | | | Depression | POMS | 63% | .741 |
| | | | | | Anger | POMS | 82% | 1.157 |
| | | | | | Fatigue | POMS | 69% | .848 |
| | | | | | Confusion | POMS | 51% | .563 |
| | | | | | Total Mood Disturbance | POMS | 65% | .775 |
| Smith ³⁹ | Alcohol | 24 | 23 | Double Blind | Total Mood Disturbance | POMS | 62% | .725 |
| Weingarten ⁴⁰ | Alcohol | 12 | 12 | Single Blind | Anxiety | POMS | 58% | .662 |
| | | | | | Depression | POMS | 71% | .887 |
| | | | | | Confusion | POMS | 58% | .662 |
| Totals | | 335 | 245 | | | Mean Zr Score | | .746 |

N weighted r Effect Size = .65±.08

be it depression, anxiety, anger, fatigue, mental confusion, or P300 speed as an evoked potential in the EEG.

The .08 mean error of the effect size distribution obtained can be utilized to predict the outcome of future studies when the same or similar outcome measures are studied. From this data we can suggest that in 99 out of the next 100 meta-analyses that may be completed in the future, the mean effect size will be expected to fall between $r=.42$ and $r=.88$, (the confidence limits), reflecting moderate to very strong effect sizes.

CES Procedures for Addiction Treatment: Special Considerations

When used for addiction, CES is usually applied more often and with a stronger current than used in other applications. Drug addicts can usually tolerate more current than non-addicts. Using the manufacturers recommendation for current, time and frequency settings, CES treatment may be administered anywhere from around-the-clock for the first one to three weeks to four times daily for that critical initial phase. After that, it can be slowly weaned down to a more normal schedule of use over a six week period culminating with treatments two or three times per week and on an as-needed basis to help with major stressors.

Conclusion

In this review and meta-analysis, a wide range of symptoms showed positive responses from CES treatment. In fact, CES studies targeted many of the major symptoms seen in the substance abstinence syndrome—all of which are consistent with a sympathetic nervous system dominant or overflow state. The studies reviewed here also suggest that within as little as three weeks of daily treatment, CES can go a long way towards reestablishing normal short term memory after the typical memory loss suffered by substance abusers. In contrast, it usually takes at least two years of total sobriety to show signs of significant recovery without CES intervention.^{19,35,37} CES is a safe, efficacious, cost-effective intervention for addictions. As such, CES should be added to all addiction treatment programs.

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