Cranial Electrotherapy Stimulation

Presentation to FDA Neurology Panel

February, 2012

Subjects to be Covered

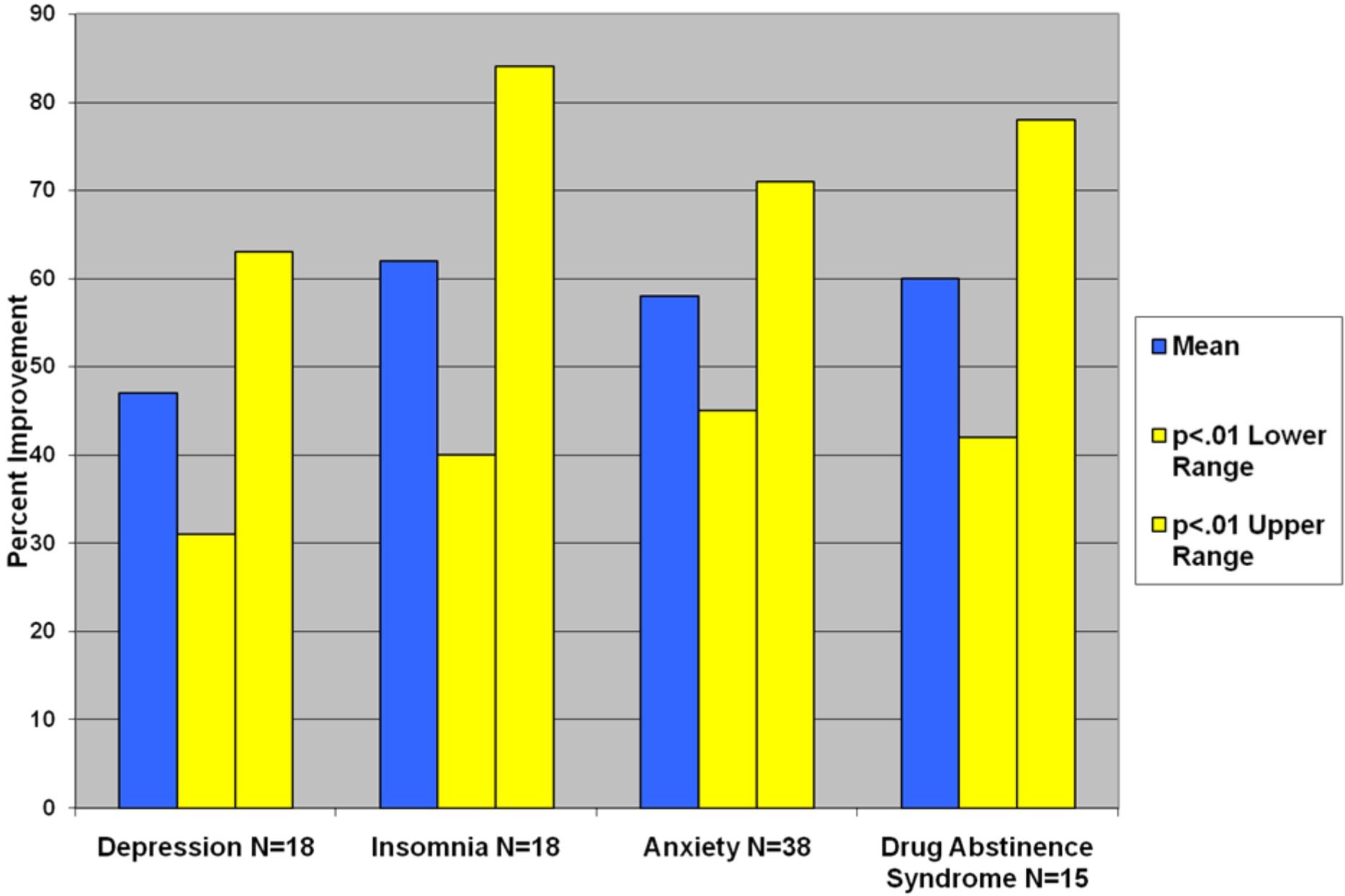
1. SUMMARY OF STUDIES
2. SUMMARY OF ADDICTION STUDIES
3. BLOOD PLASMA AND CSF STUDIES
4. MECHANISMS OF ACTION STUDIES
5. FOLLOW UP STUDIES
6. A LOOK AT THE SAFETY OF CES
7. RECOMMENDATIONS TO PANEL

Summary of Studies

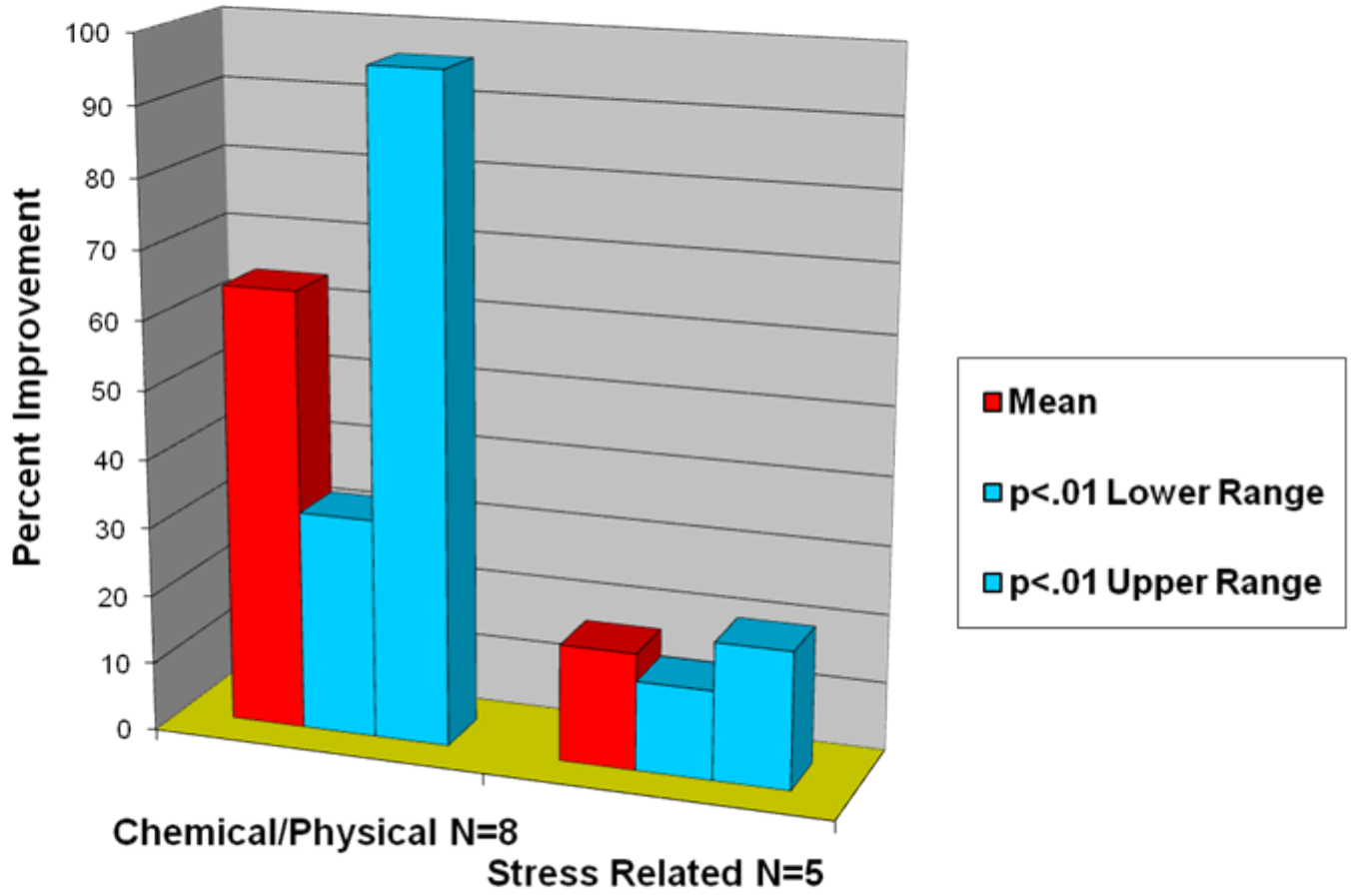
(Valid Scientific Evidence, 21 CFR 860.7 (C)(2))

1. Well Controlled Investigations
    a. Double Blind
    b. Single Blind
    c. Crossover Studies
2. Studies and objective trials without matched controls
    a. Open Clinical Trials

Treatment Effect Sizes Obtained, and Expected from Future Research



The Effect of CES Treatment on Cognitive Improvement in Different Etiologies, and Prediction of Outcomes in Future Meta-Analyses

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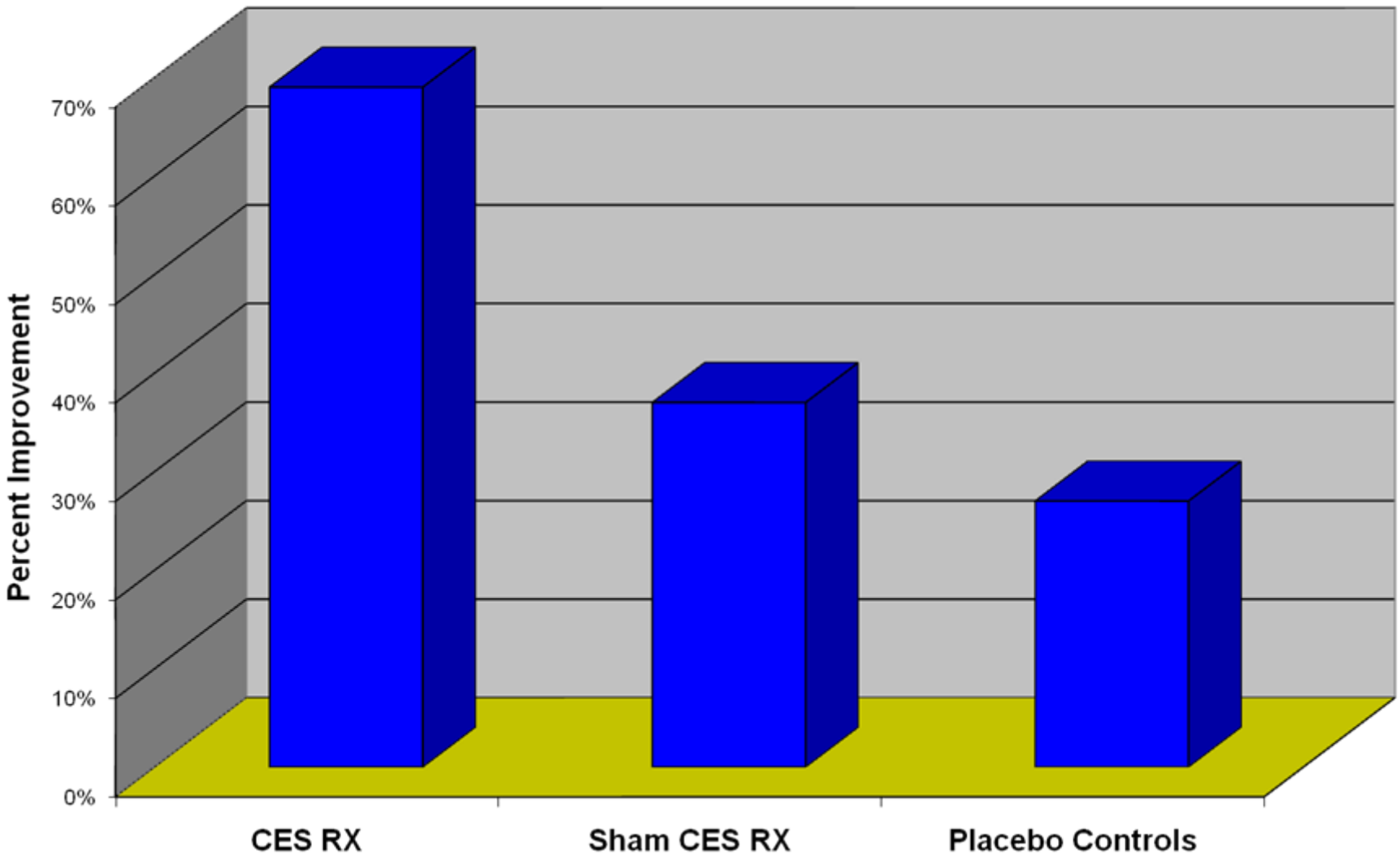
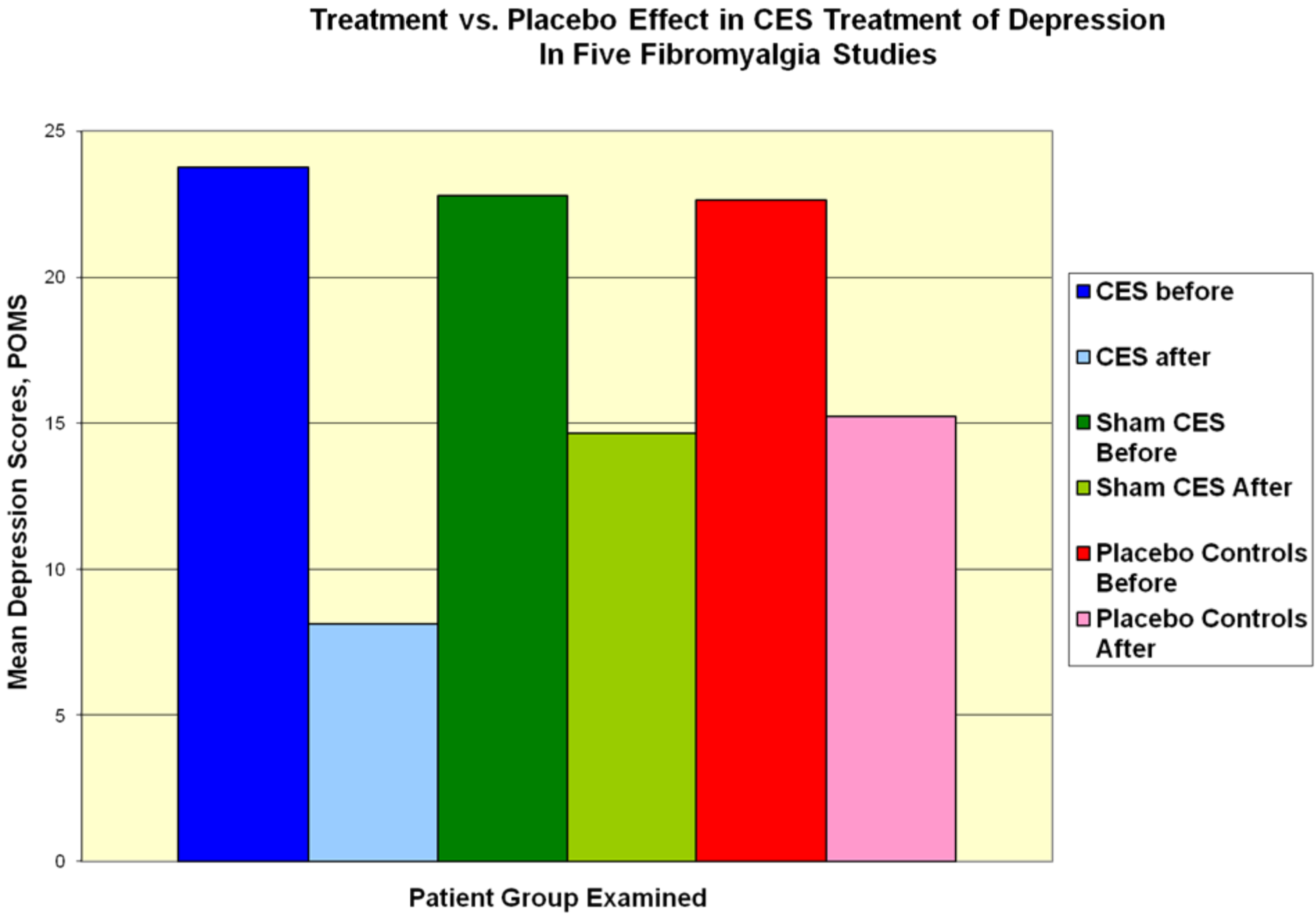
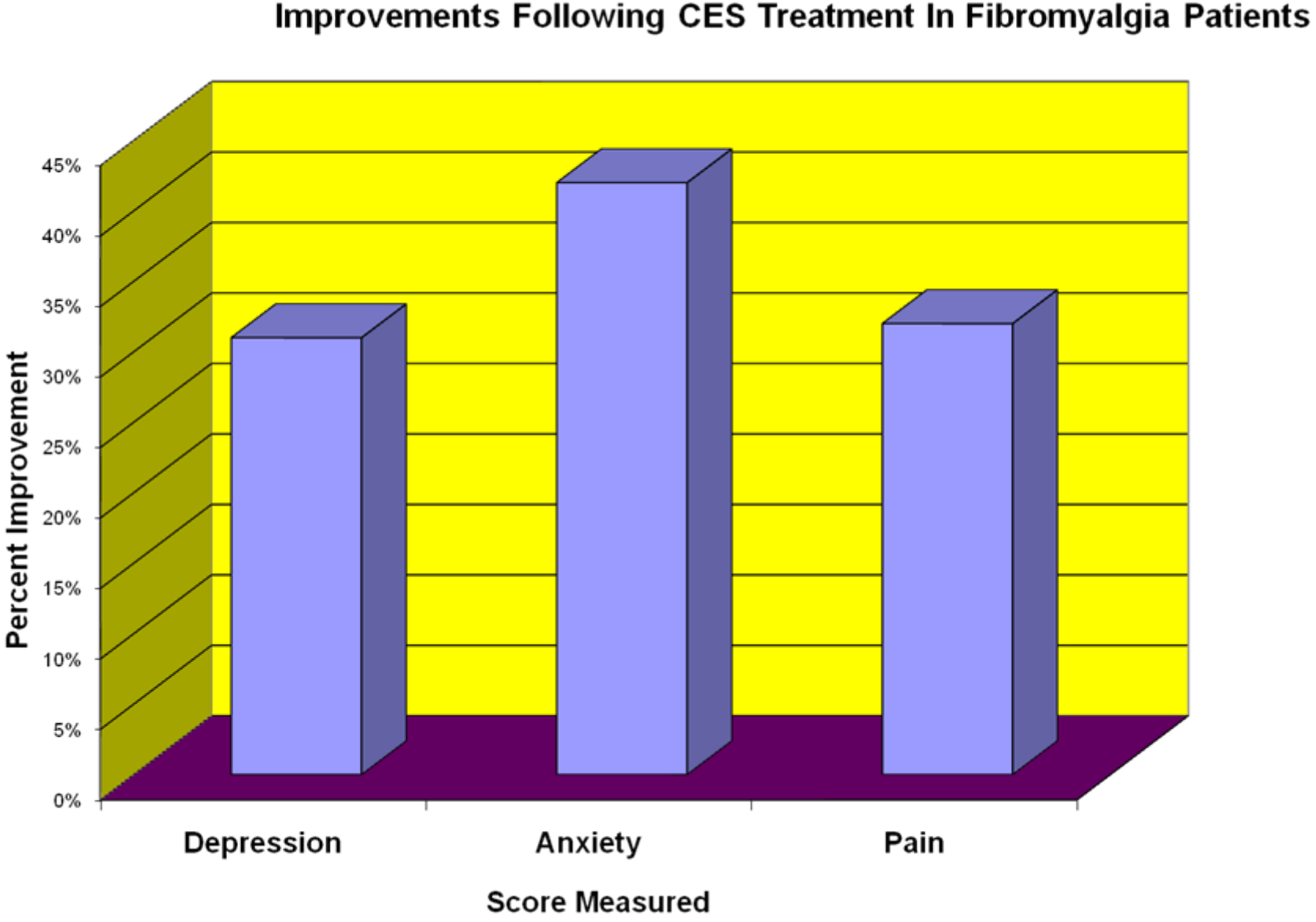
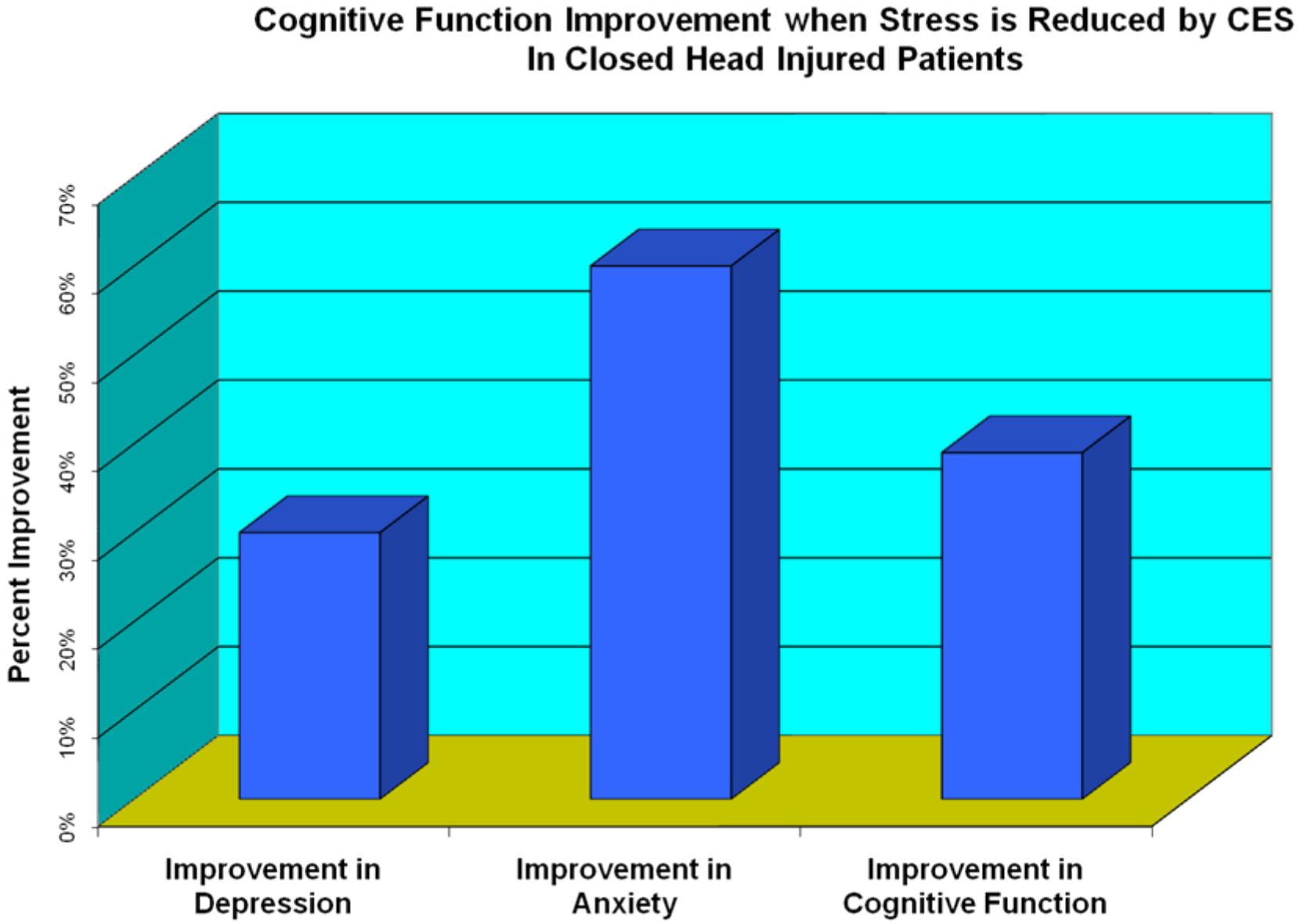
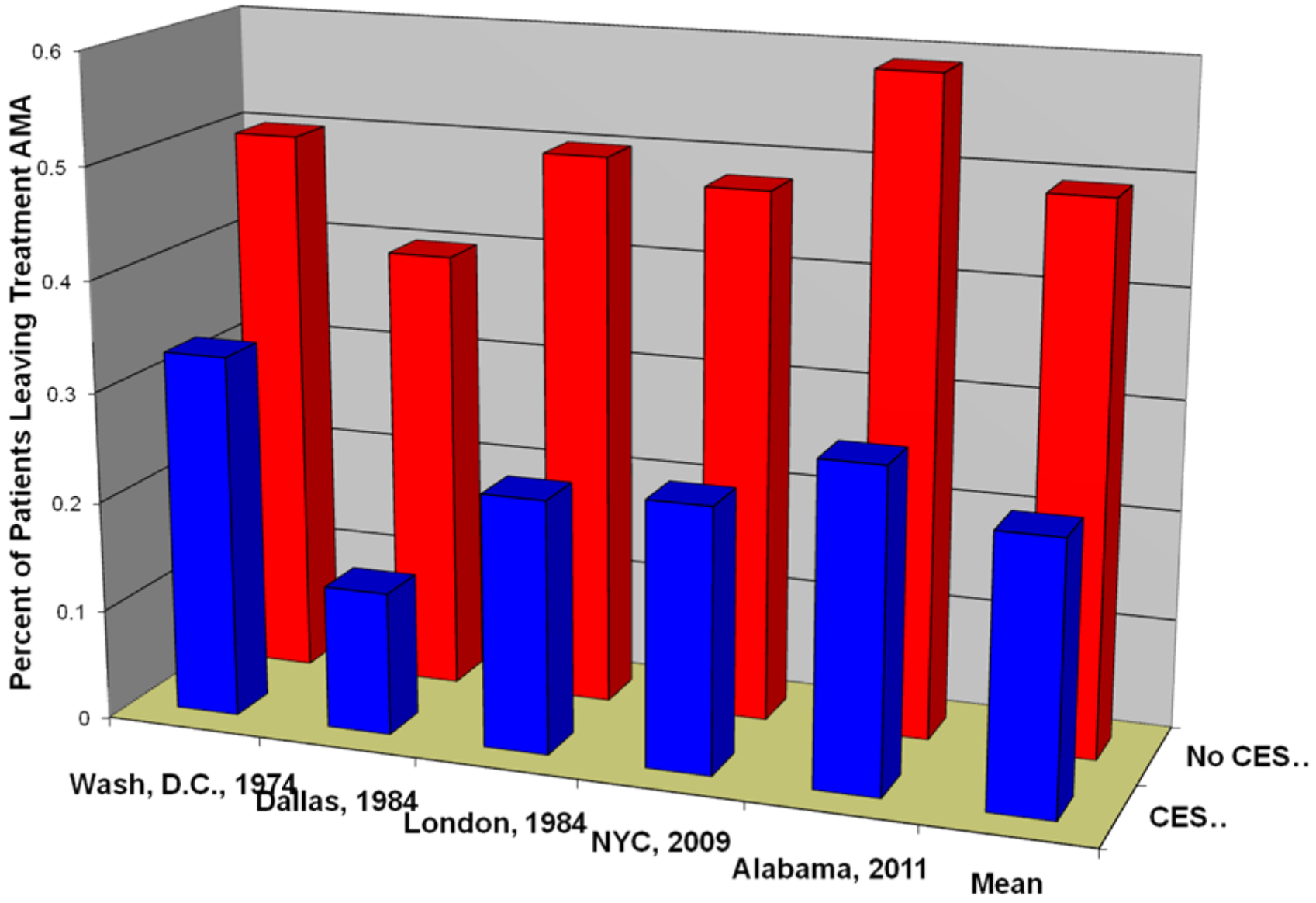

Measuring Placebo Effect in Four CES Depression Studies
Percent Improvement
70%
60%
50%
40%
30%
20%
10%
0%
CES RX
Sham CES RX
Placebo Controls

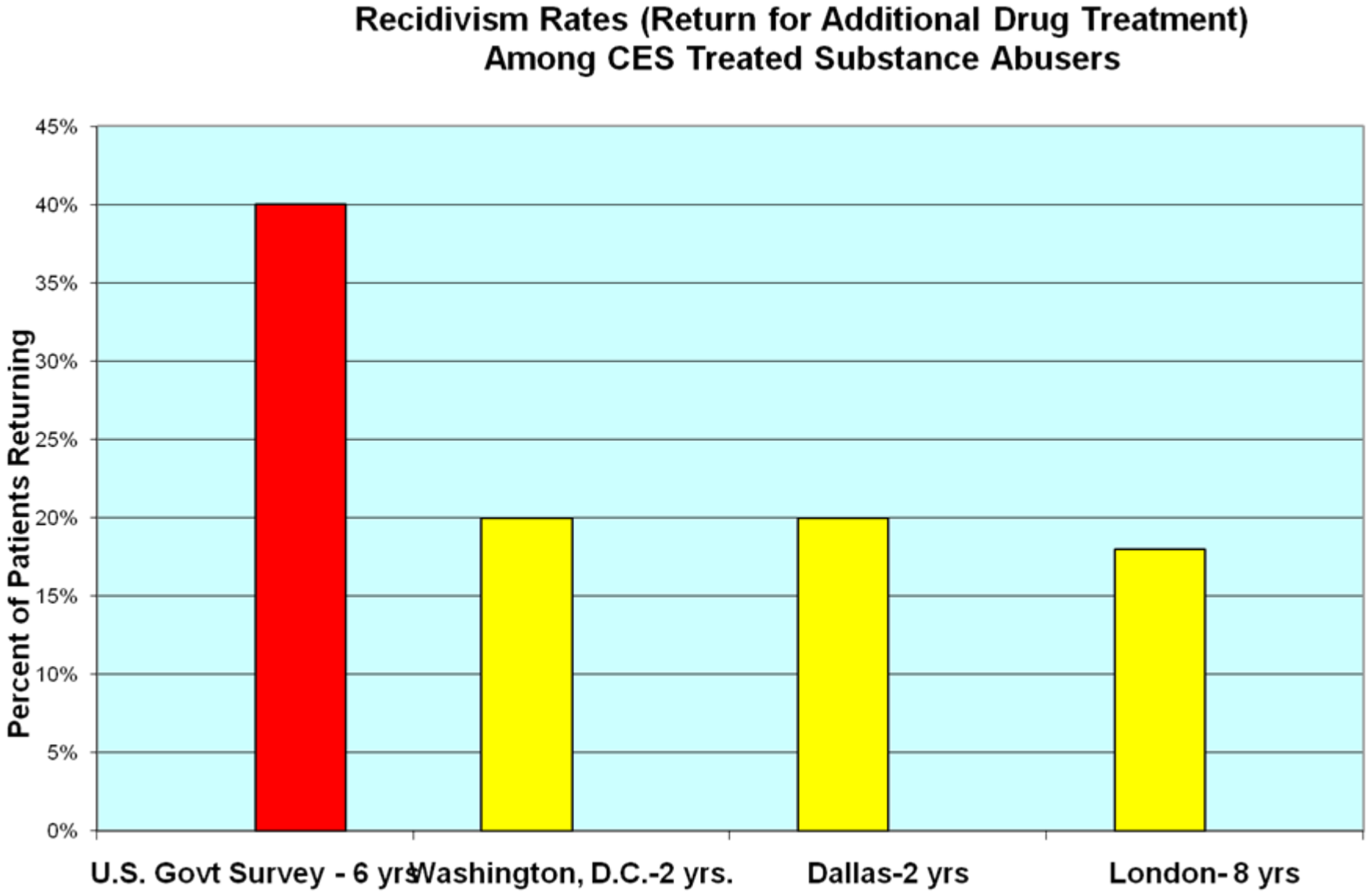

Treatment vs. Placebo Effect in CES Treatment of Depression
In Five Fibromyalgia Studies
Mean Depression Scores, POMS
25
20
15
10
5
0
Patient Group Examined
CES before
CES after
Sham CES Before
Sham CES After
Placebo Controls Before
Placebo Controls After


Improvements Following CES Treatment In Fibromyalgia Patients
Percent Improvement
45%
40%
35%
30%
25%
20%
15%
10%
5%
0%
Depression
Anxiety
Pain
Score Measured

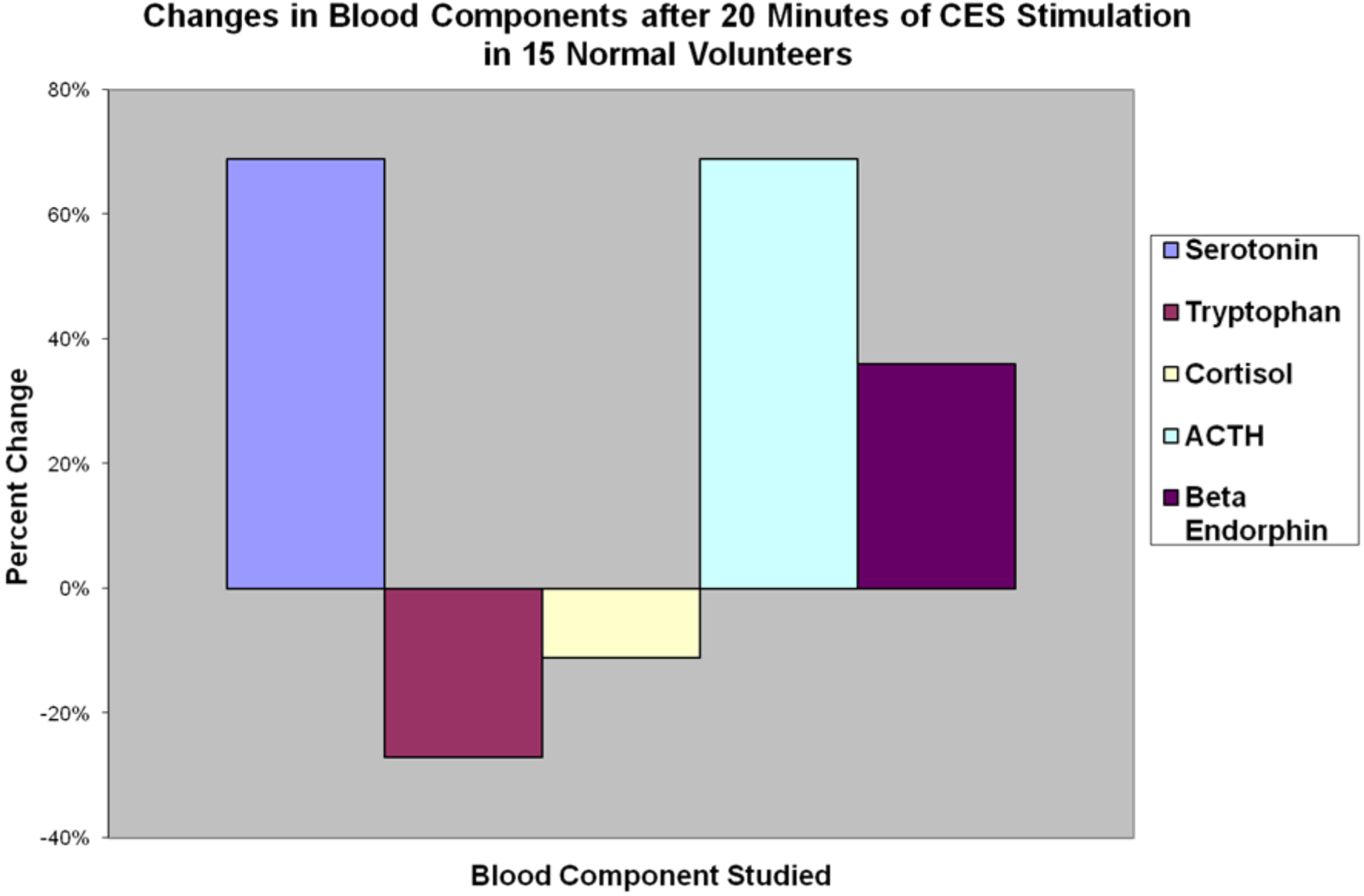

Cognitive Function Improvement when Stress is Reduced by CES
In Closed Head Injured Patients
Percent Improvement
0%
10%
20%
30%
40%
50%
60%
70%
Improvement in Depression
Improvement in Anxiety
Improvement in Cognitive Function

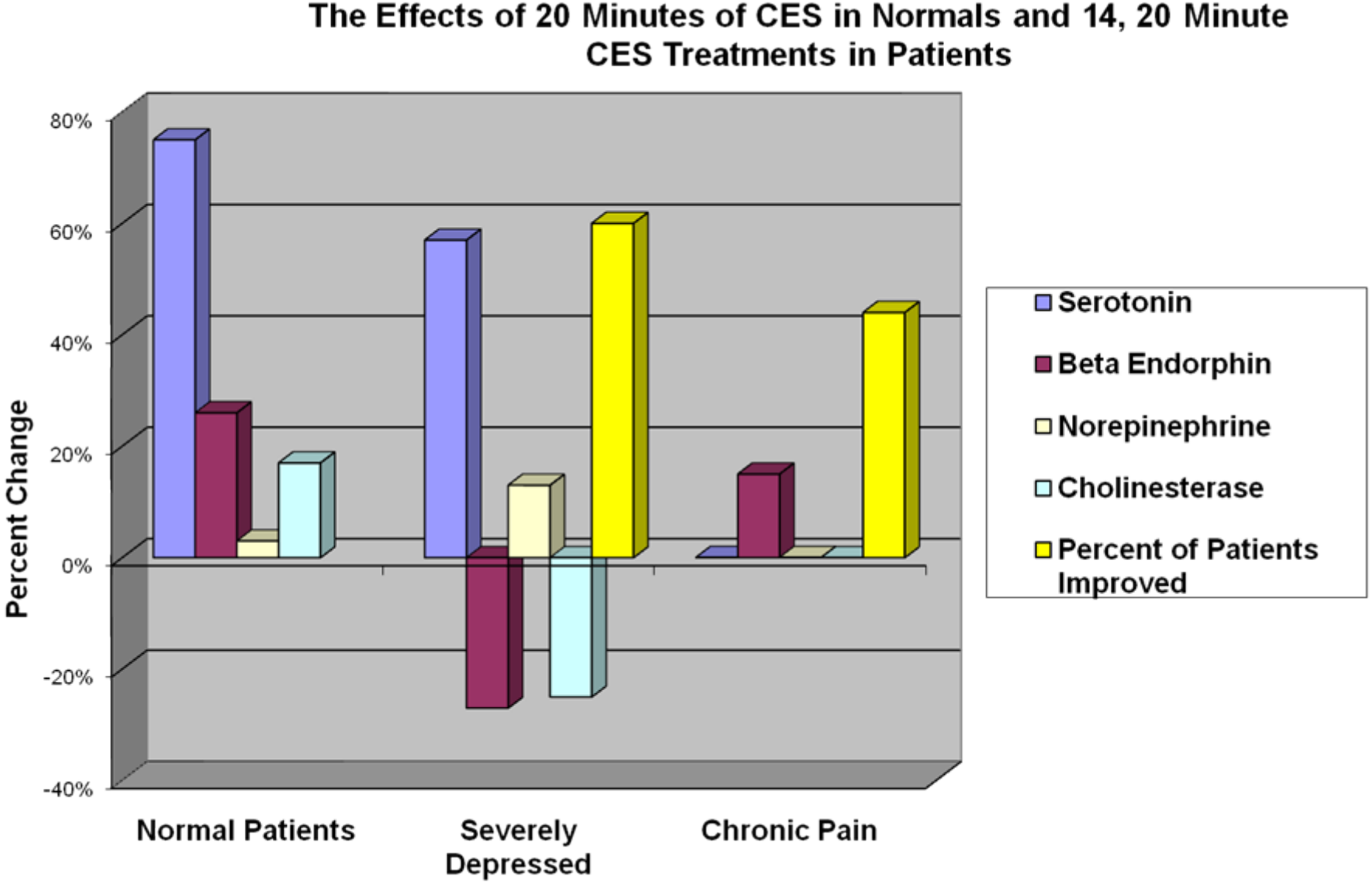
Summary of Addiction Studies


The Effect of CES Treatment on Keeping Patients in Addiction Treatment
For the Full Treatment Program
Percent of Patients Leaving Treatment AMA
0.6
0.5
0.4
0.3
0.2
0.1
0
Wash, D.C., 1974
Dallas, 1984
London, 1984
NYC, 2009
Alabama, 2011
Mean
No CES..
CES..


Recidivism Rates (Return for Additional Drug Treatment)
Among CES Treated Substance Abusers
Percent of Patients Returning
45%
40%
35%
30%
25%
20%
15%
10%
5%
0%
U.S. Govt Survey - 6 yrs
Washington, D.C.-2 yrs.
Dallas-2 yrs
London- 8 yrs

Blood and CSF Studies

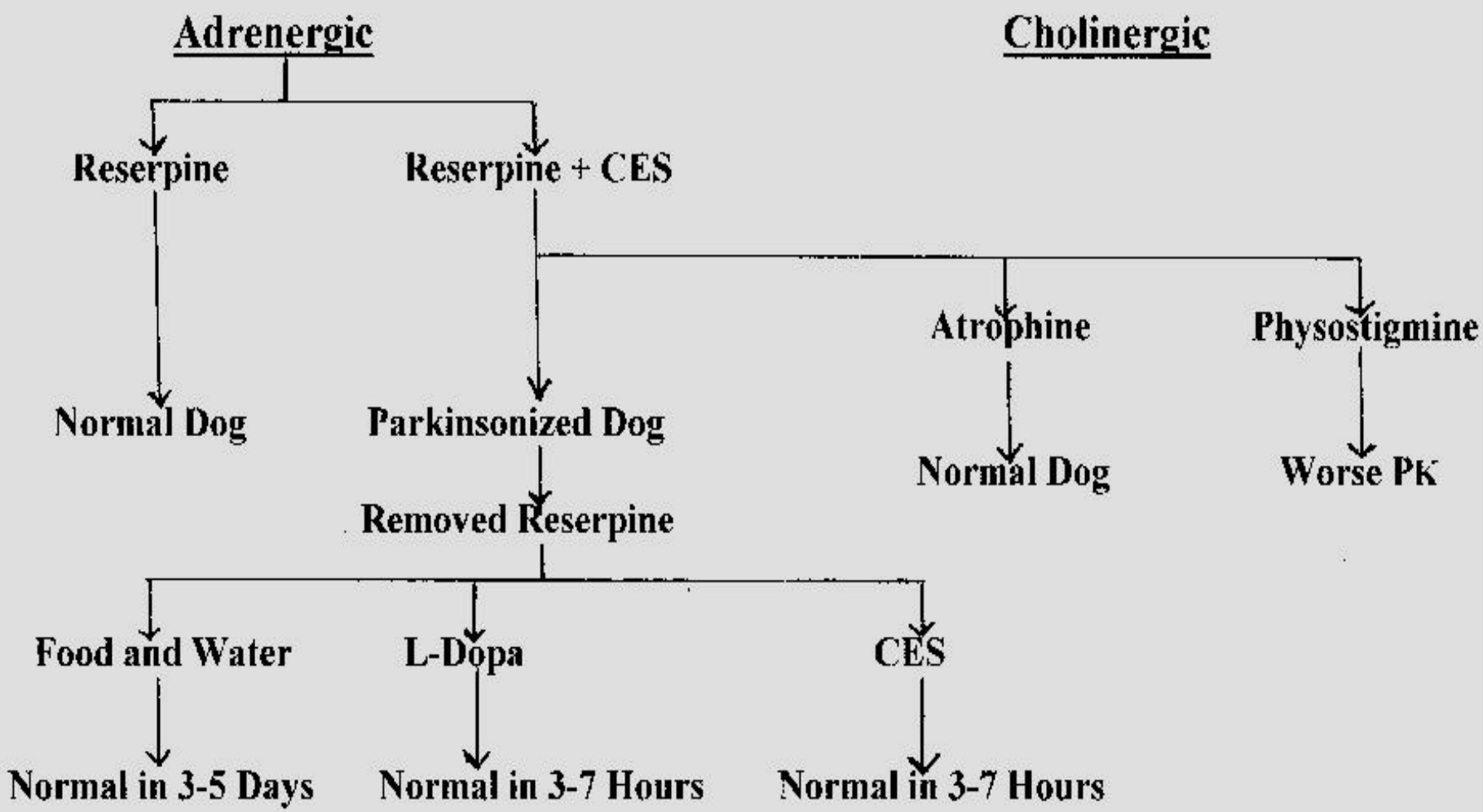

Changes in Blood Components after 20 Minutes of CES Stimulation in 15 Normal Volunteers
80%
60%
40%
20%
0%
-20%
-40%
Percent Change
Blood Component Studied
Serotonin
Tryptophan
Cortisol
ACTH
Beta Endorphin


The Effects of 20 Minutes of CES in Normals and 14, 20 Minute CES Treatments in Patients
Percent Change
80%
60%
40%
20%
0%
-20%
-40%
Normal Patients
Severely Depressed
Chronic Pain
Serotonin
Beta Endorphin
Norepinephrine
Cholinesterase
Percent of Patients Improved

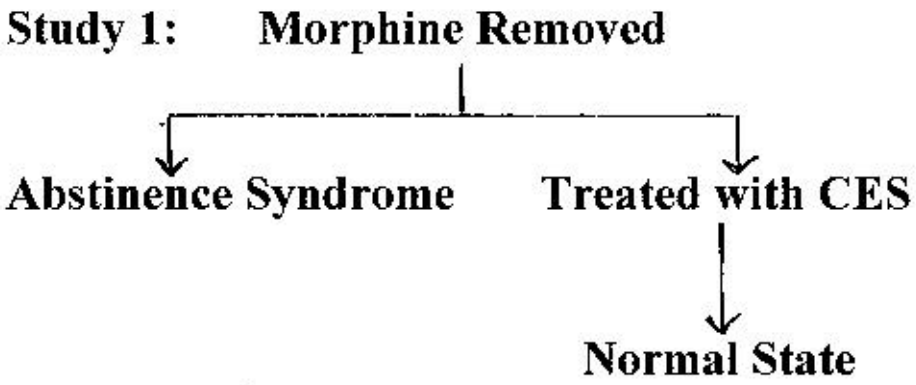
Studies of the Mechanism of Action

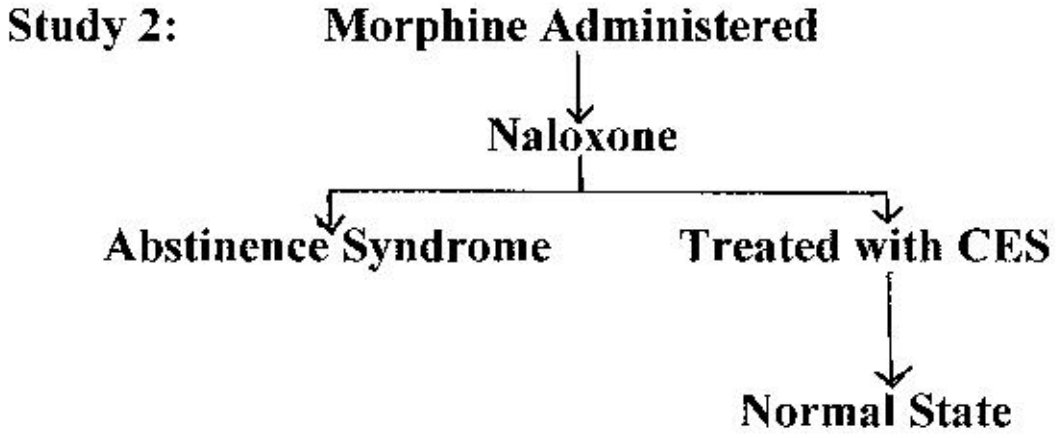
Dr. Pozos Sought to See if CES Stimulates Dopamine in the Brain of Dogs

He Looked at the Balance Between the Adrenergic and Cholinergic Systems in the Brain

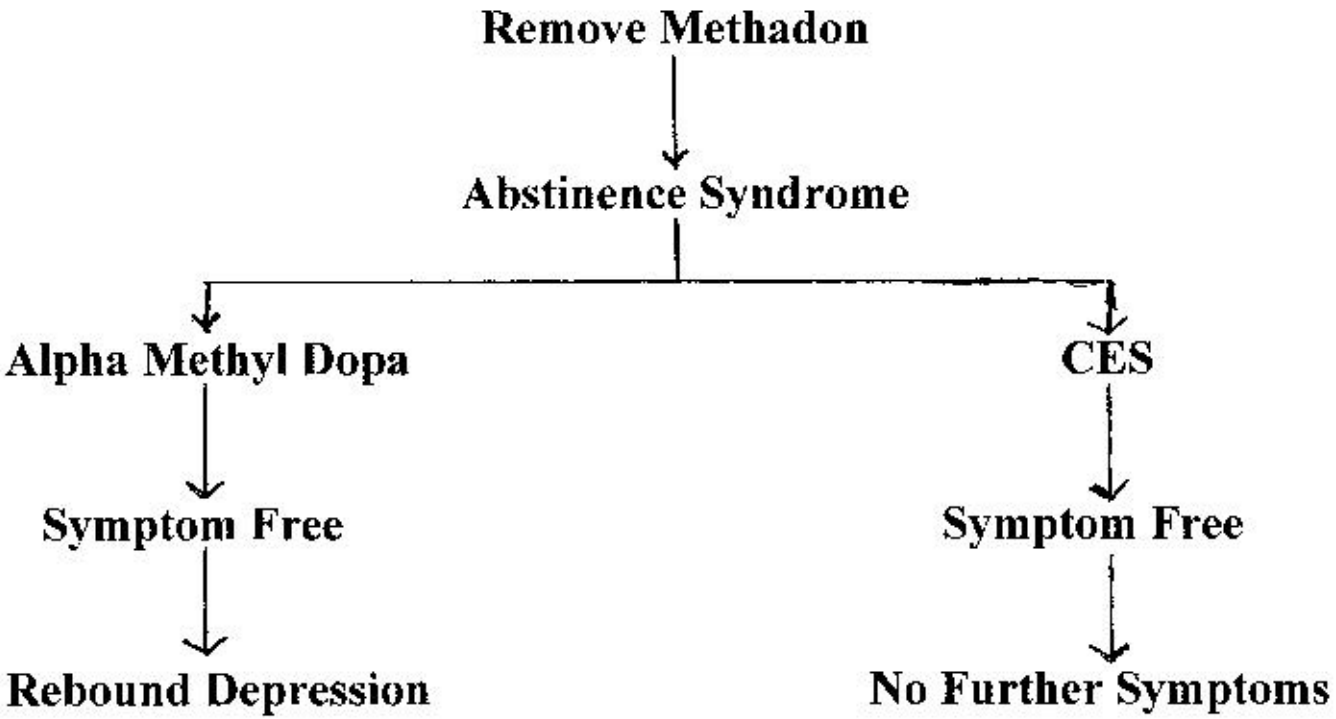


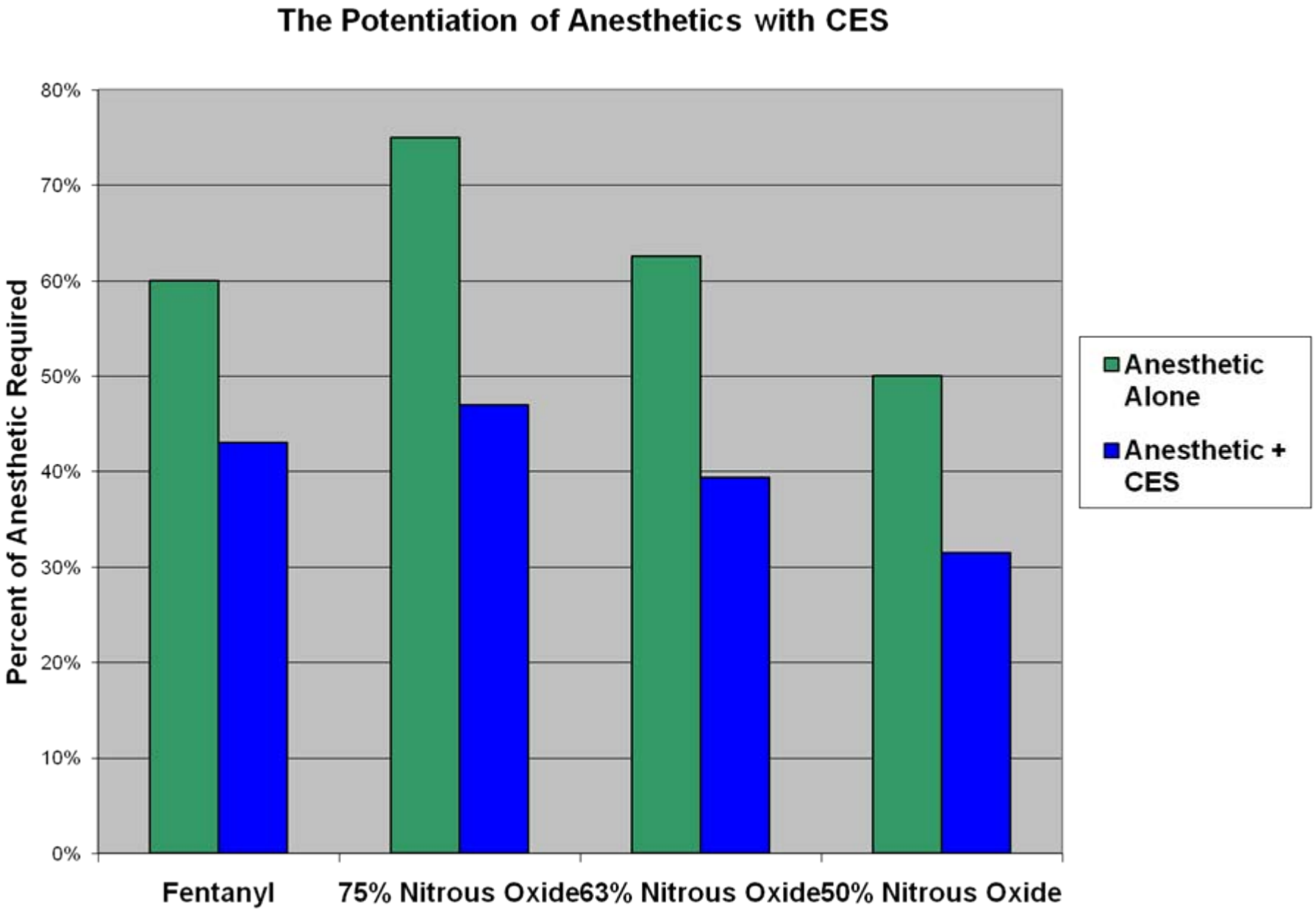
Dougherty Studied The Effects of CES in Morphine Addicted Rats



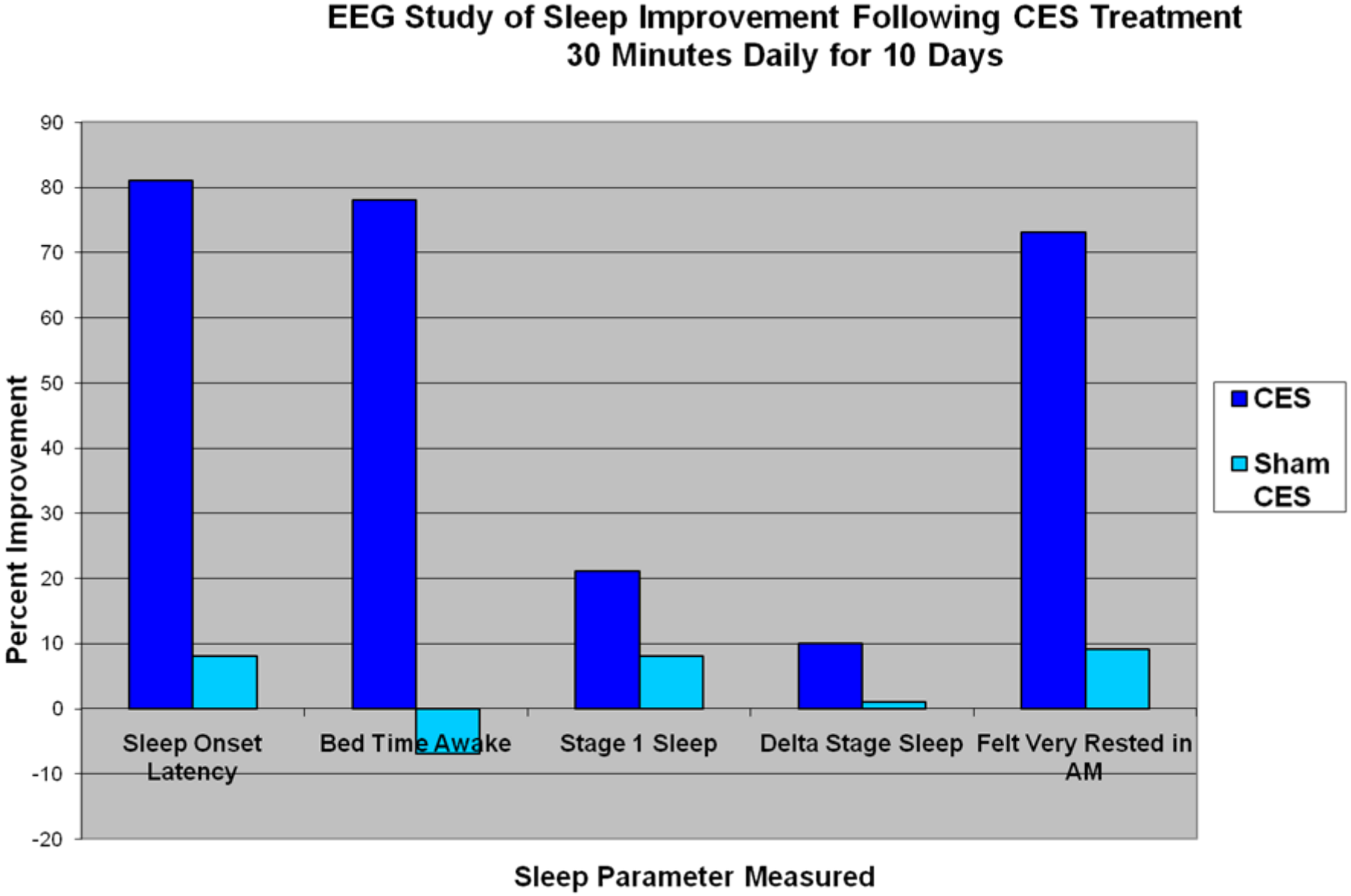


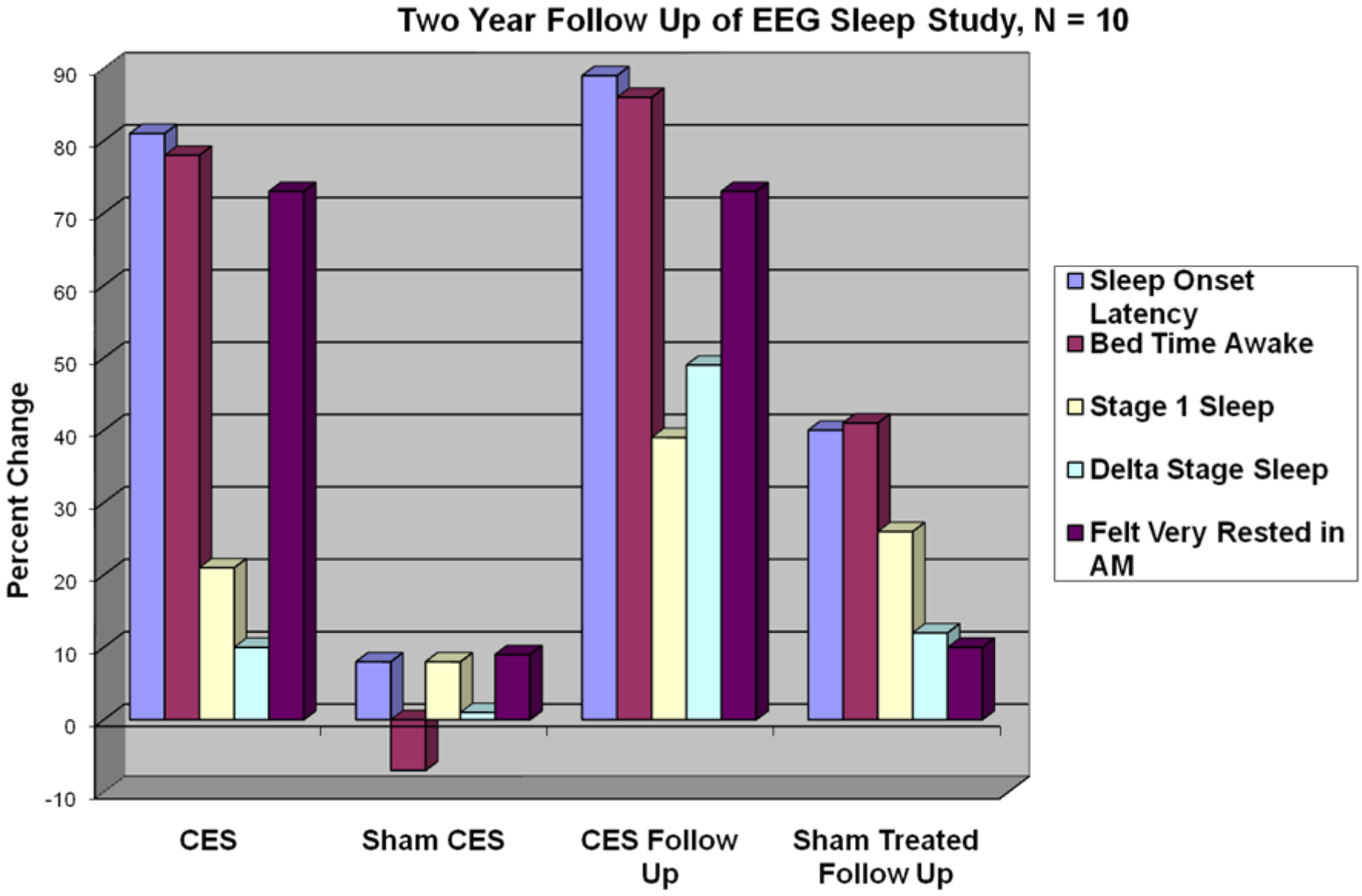
Dr. Mark Gold Studied the Effects of CES Treatment With Heroin Addicts Withdrawing from Methadon In His Clinic in New Jersey

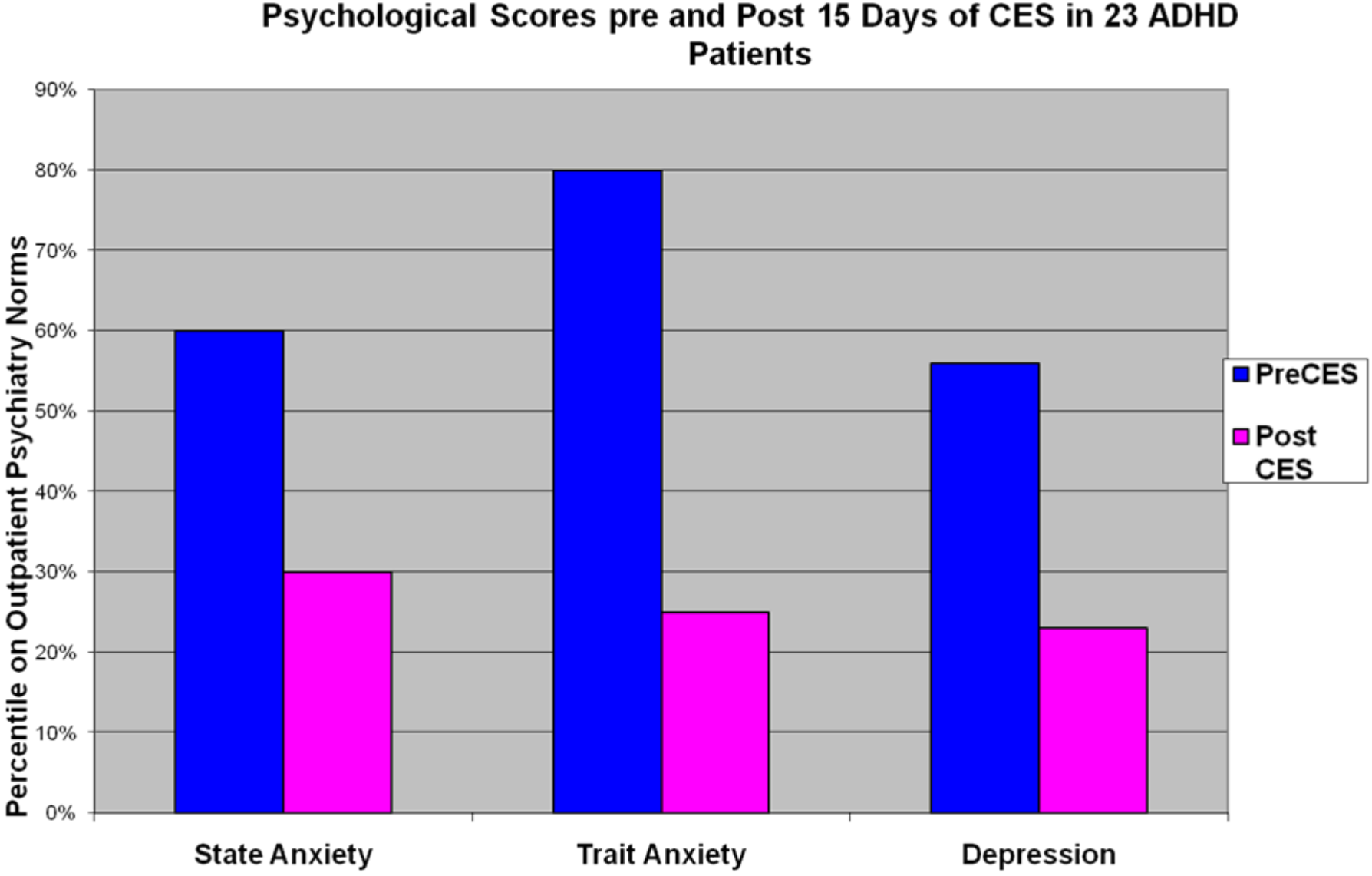


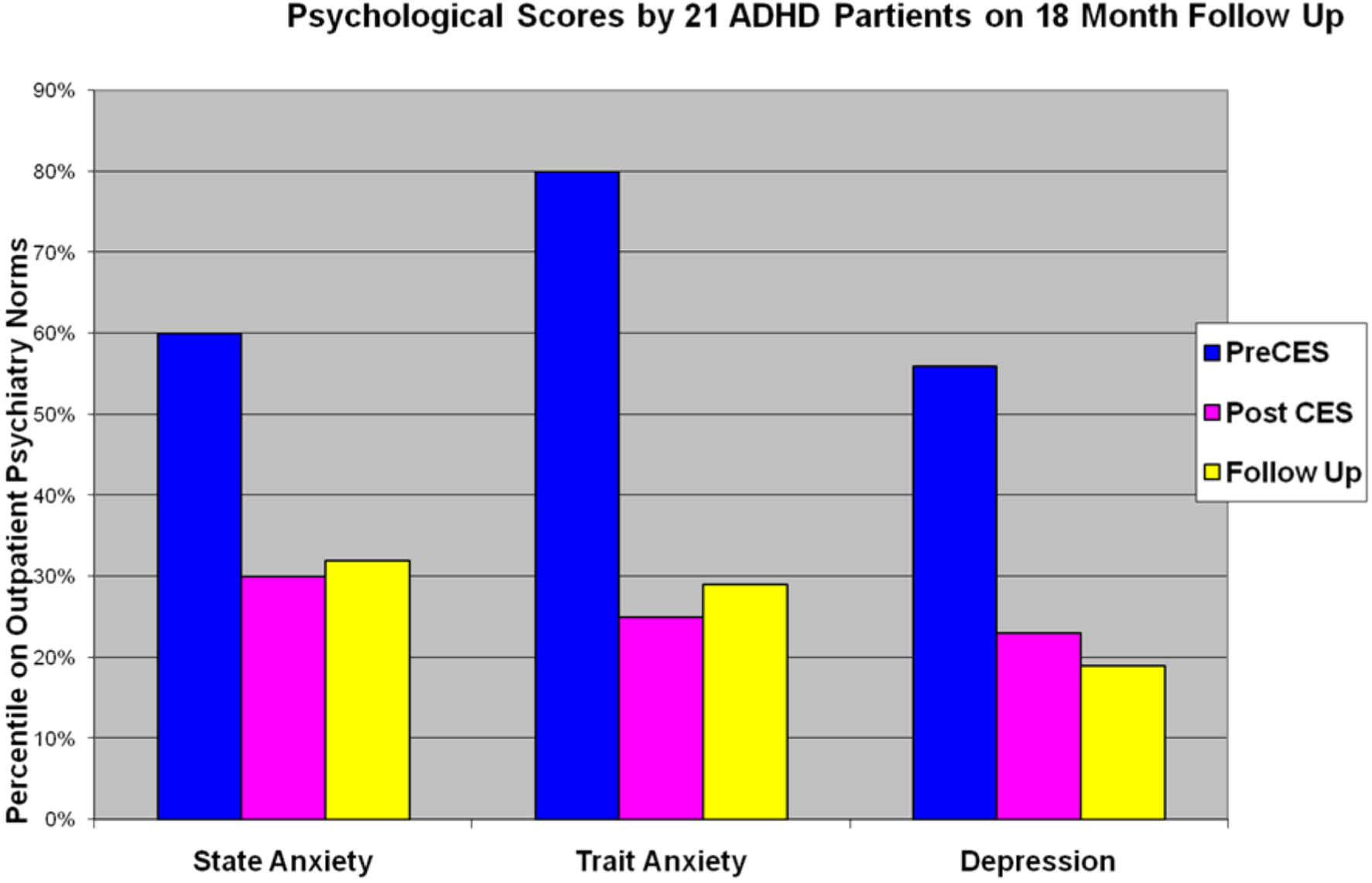

The Potentiation of Anesthetics with CES
Percent of Anesthetic Required
80%
70%
60%
50%
40%
30%
20%
10%
0%
Fentanyl
75% Nitrous Oxide
63% Nitrous Oxide
50% Nitrous Oxide
Anesthetic Alone
Anesthetic + CES

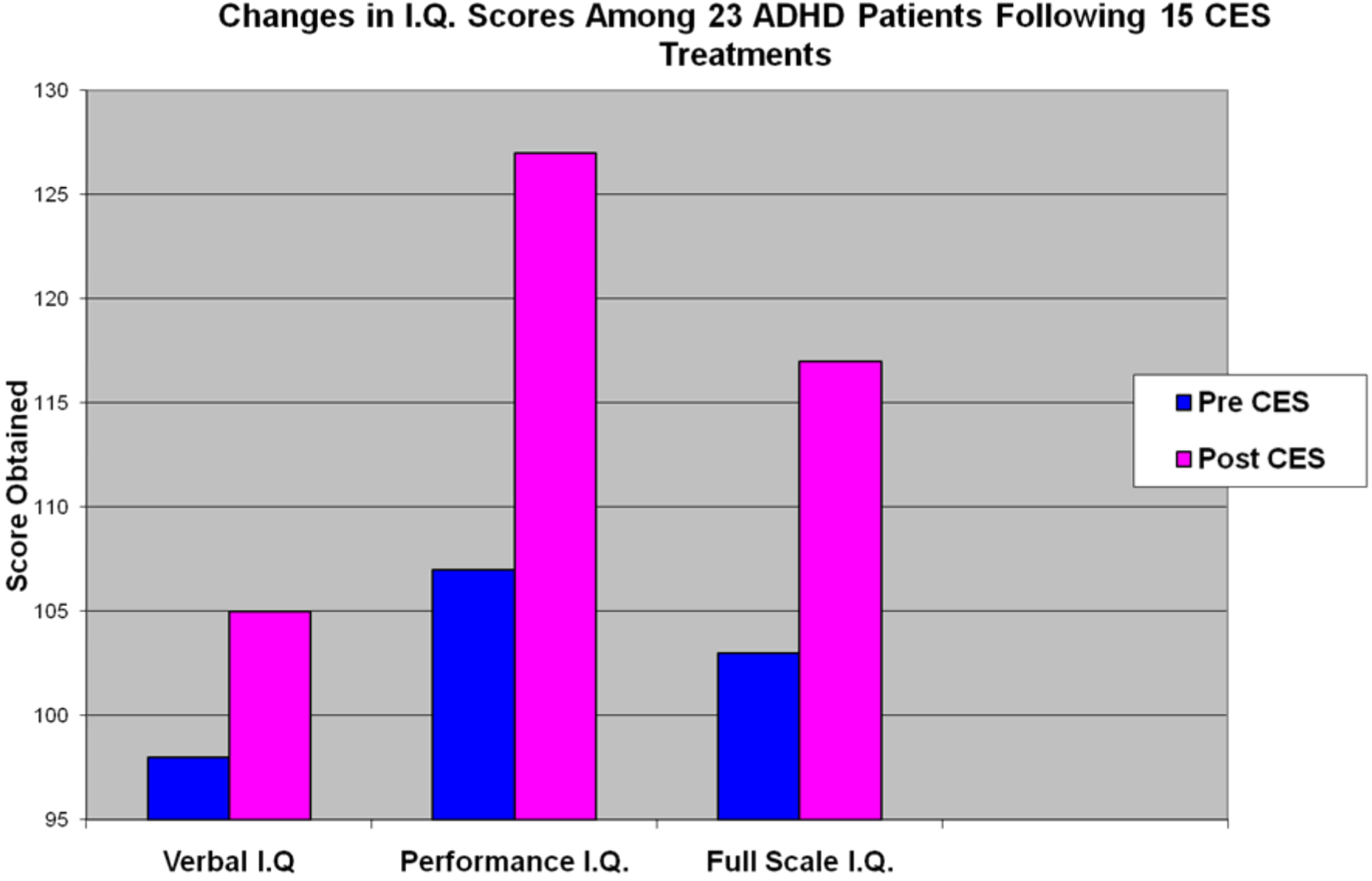
Follow Up Studies

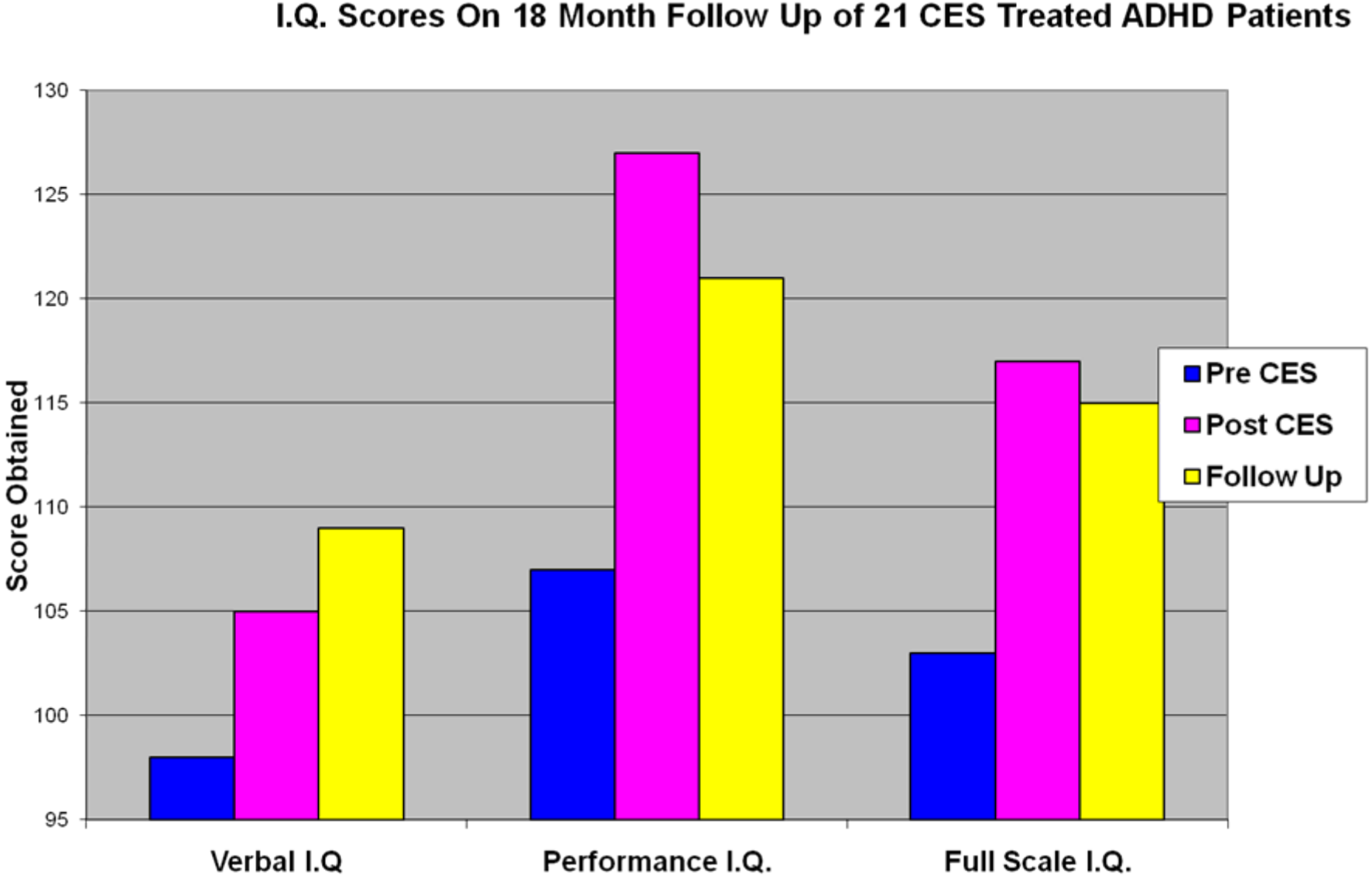

EEG Study of Sleep Improvement Following CES Treatment
30 Minutes Daily for 10 Days
Percent Improvement
90
80
70
60
50
40
30
20
10
0
-10
-20
Sleep Onset Latency
Bed Time Awake
Stage 1 Sleep
Delta Stage Sleep
Felt Very Rested in AM
Sleep Parameter Measured
CES
Sham CES


Two Year Follow Up of EEG Sleep Study, N = 10
Percent Change
90
80
70
60
50
40
30
20
10
0
-10
CES
Sham CES
CES Follow Up
Sham Treated Follow Up
Sleep Onset Latency
Bed Time Awake
Stage 1 Sleep
Delta Stage Sleep
Felt Very Rested in AM


Psychological Scores pre and Post 15 Days of CES in 23 ADHD Patients
Percentile on Outpatient Psychiatry Norms
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
State Anxiety
Trait Anxiety
Depression
PreCES
Post CES


Psychological Scores by 21 ADHD Partients on 18 Month Follow Up
Percentile on Outpatient Psychiatry Norms
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
State Anxiety
Trait Anxiety
Depression
PreCES
Post CES
Follow Up

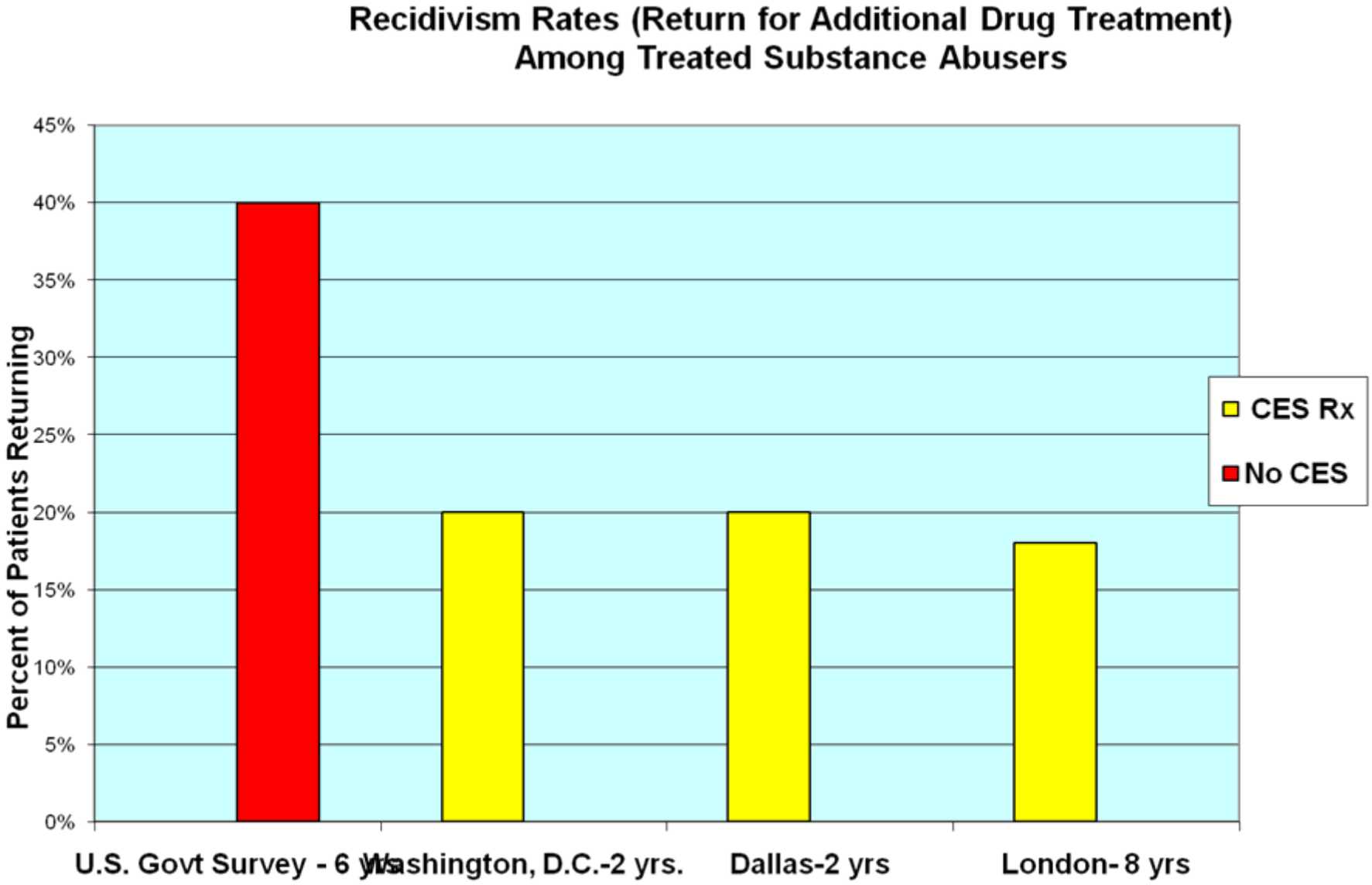

Changes in I.Q. Scores Among 23 ADHD Patients Following 15 CES Treatments
Score Obtained
130
125
120
115
110
105
100
95
Verbal I.Q
Performance I.Q.
Full Scale I.Q.
Pre CES
Post CES


I.Q. Scores On 18 Month Follow Up of 21 CES Treated ADHD Patients
Score Obtained
130
125
120
115
110
105
100
95
Verbal I.Q
Performance I.Q.
Full Scale I.Q.
Pre CES
Post CES
Follow Up

The Safety of CES

In the treatment of more than 100,000 patients in the U.S. with CES there has never been a seizure reported.

This was true even among known seizure patients such as withdrawing addicts and closed head injured subjects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Among Treated Substance Abusers
Percent of Patients Returning
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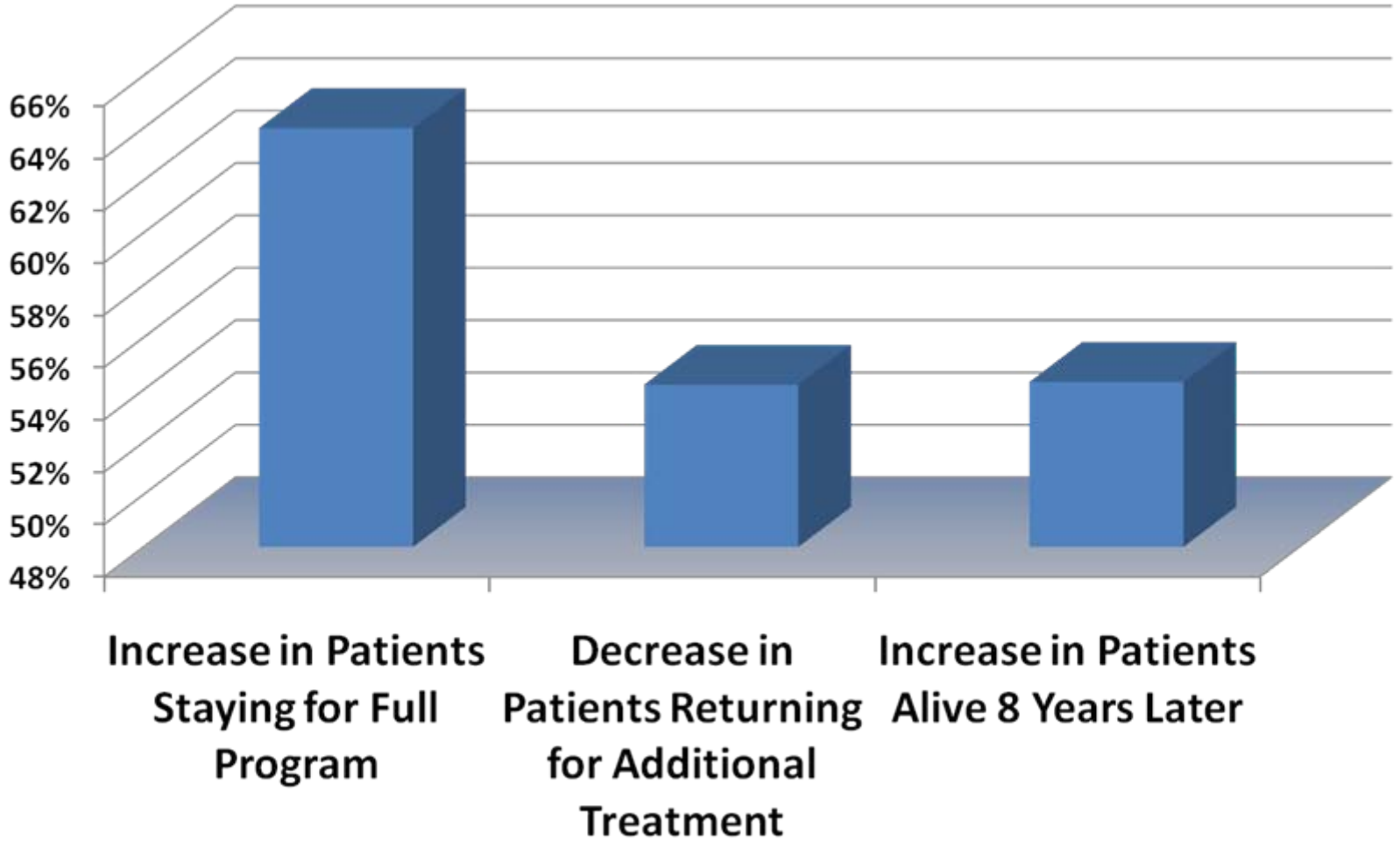
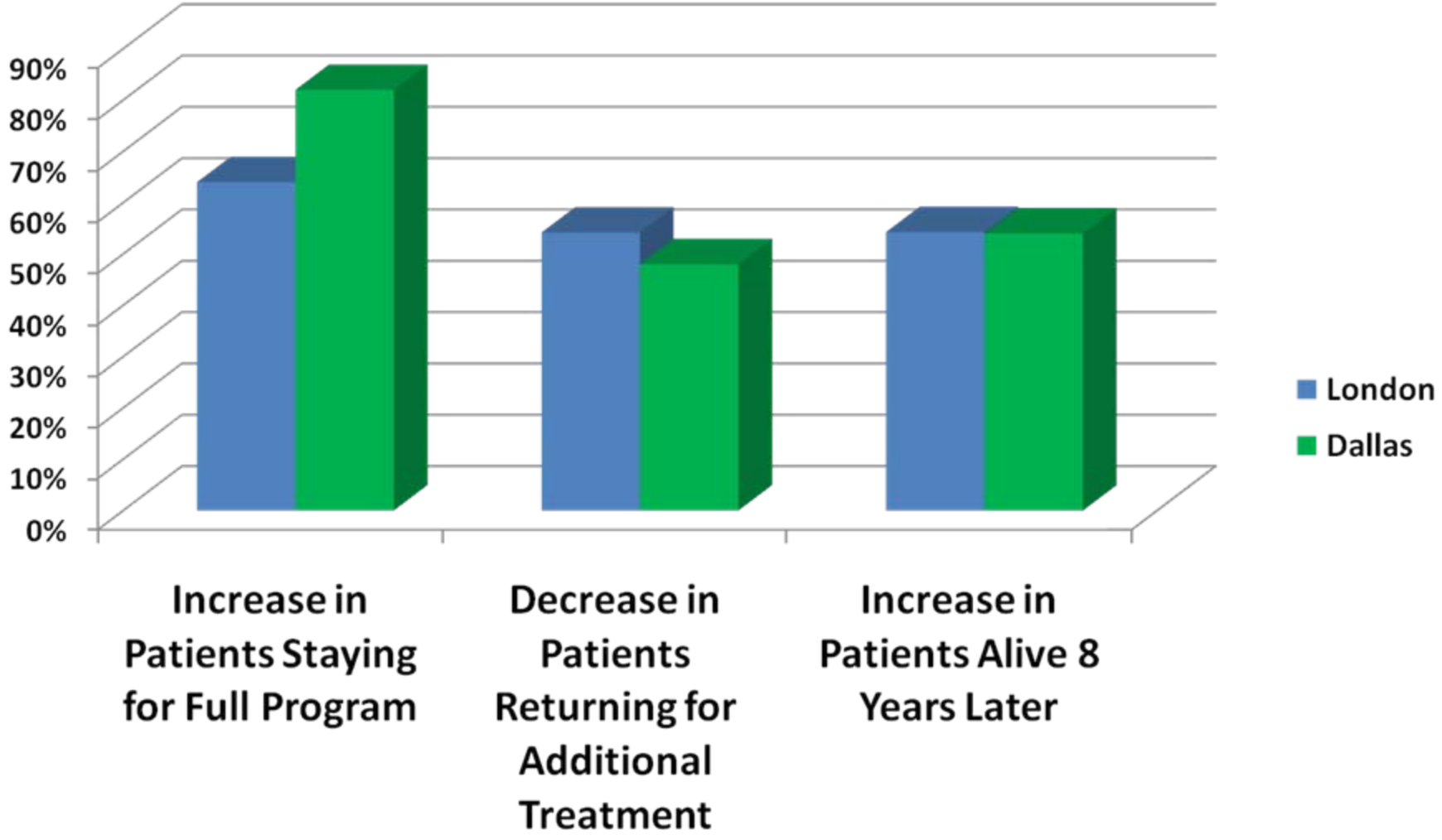
5%
0%
CES Rx
No CES
U.S. Govt Survey - 6 yrs
Washington, D.C.-2 yrs.
Dallas-2 yrs
London- 8 yrs

CES Patients Compared With London Norms for Non CES Treated Patients



Comparable Patient Statistics Between London and Dallas CES Addiction Treatment Programs



Recommendations

CES Be Classified in Class II for

1.Stress:

- **A. Depression**
- **B. Anxiety**
- **C. Insomnia**
- **D. Cognitive Dysfunction**

2. Treatment of Addiction

3. Adjunctive Treatment for Pain