# CRANIAL ELECTROTHERAPY STIMULATION (CES)

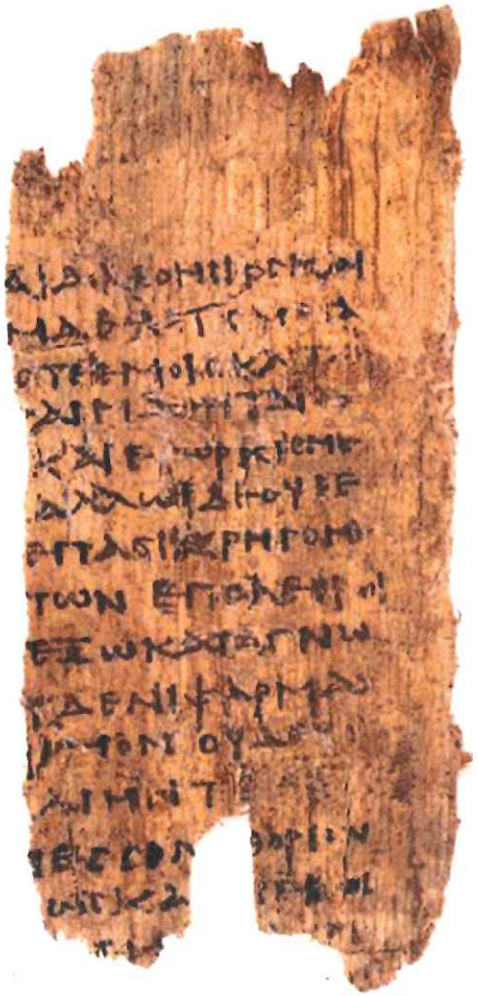
## and the treatment of

## Depression, Anxiety & Insomnia


Charles A. Fisher

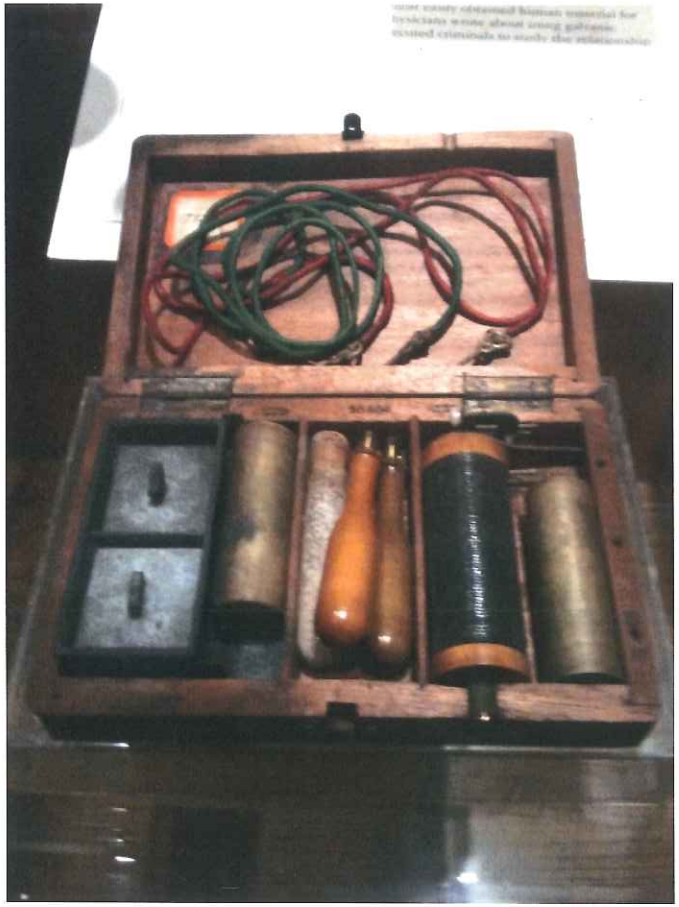
President, Fisher Wallace Laboratories

# Humble Beginnings of CES



- 46 AD – Scribonius Largus
  - Black Torpedo Fish
- 1700's – Charles Kite
  - Electric Defibrillator
- 1850's – Strange Contraptions

# Early Devices




* Electro-medical apparatus, A. Gaiffe, Paris 1868

# CES Today


- FDA-Cleared since 1976 for depression, anxiety & insomnia
- Track record of safety
- Scores of published studies, particularly in substance abuse arena
- Portable & battery powered
- Easy-to-Use
- Three key frequencies

# Mechanism of Action

- Increases Serotonin*
- Increases Beta-Endorphins*
- Increases GABA*
- Decreases Cortisol*
- Decreases in Neuronal Activity

  Unlike tDCS, CES does not polarize the brain. The effects of cranial AC stimulation have been shown to decrease neuronal activity, which may explain reduction in anxiety.

* Proven in blood, cerebral spinal fluid & saliva tests published in peer reviewed journals

# Ease of Use

- 20 minutes Treatment Session
  - Shuts Off Automatically
  - One Moving Part
- 30-45 Ideal Treatment Period
- Use with or without medication
- Out-patient, in-patient & home-care
- Low cost and few replaceables

# Very Low Risk

- Decades of clinical use and many published studies without adverse events
- No serious side effects
- No contraindications with medication
- Stimulation is far below seizure threshold
- 100X less amperage than TMS and 1000X less than ECT
- Battery powered – Two AA
- AC current = no electrode burns (v. tDCS)

# Effectiveness

- Research averages 65% - 70%
- Often eliminates insomnia in first week of use
- Often reduces depression and anxiety within two weeks of use
- May be used in conjunction with medication to lower dosage and thus lower medication side effects

# PTSD

**"The Cranial Electrotherapy Stimulator (CES)... stimulates the parasympathetic part of the nervous system which counteracts the stress response, thus reducing the physical symptoms of PTSD such as rapid pulse, shaking, sweating, or a knot in the stomach. It also addresses psychological symptoms by reducing anxiety, restlessness, agitation, anger, depression, and sleep problems. Furthermore, the improvements in emotion regulation reduce the risk of inappropriate impulsive, aggressive behaviors."**

- Richard Brown, MD
  Associate Professor in Clinical Psychiatry
  Columbia University College of Physicians and Surgeons

# Summary

**PROS:** Human and animal randomized studies show clinically effective and statistically significant reductions (and remission) in insomnia, depression and anxiety symptoms in selected populations following cranial stimulation. Human studies provide evidence that cranial stimulation produces changes in biochemical components in blood and cerebral spinal fluid that may be associated with the clinical changes found in the randomized studies. No reports of adverse events.

**CONS:** Many studies are older, of small subject size (but still statistically significant), varying patient populations, and employ different CES dosing.

# Addiction Recovery Pilot Program

Phoenix House
Rising Above Addiction

- Largest non-profit drug rehab center in USA
- 392 Subjects – cocaine and heroine addicts
  - 293 Non-CES (control)
  - 99 CES (for first 10 days of detox)
- PTSD & detox symptoms: depression, anxiety, insomnia

# Phoenix House – Outcome

- **50% increase in retention after 90 days** (versus control group)

- Reported profound reduction of PTSD & detox symptoms (anxiety & insomnia)

Table 2. *Comparison of attrition rates between clients who received CES and clients who did not receive CES.*

| Residential treatment attrition | no CES<br>n = 293 | received CES<br>n = 99 |
|---|---|---|
| | n (%) | n (%) |
| at day 7 | 29 (9.9) | 0 (0.0) |
| at day 14 | 62 (21.2) | 3 (3.0) |
| at day 30 | 89 (30.4) | 10 (10.1) |
| at day 60 | 120 (41.0) | 17 (17.2) |
| at day 90 * | 131 (48.3) | 23 (24.0) |

* *Note:* Sample sizes were n=271 and n=96 for the no-CES and CES groups respectively. Excluded from 90 day attrition analyses are 8 clients who completed residential treatment between 60 and 90 days, and 17 clients admitted at the end of May 2009 who have not reached the 90 day timepoint.

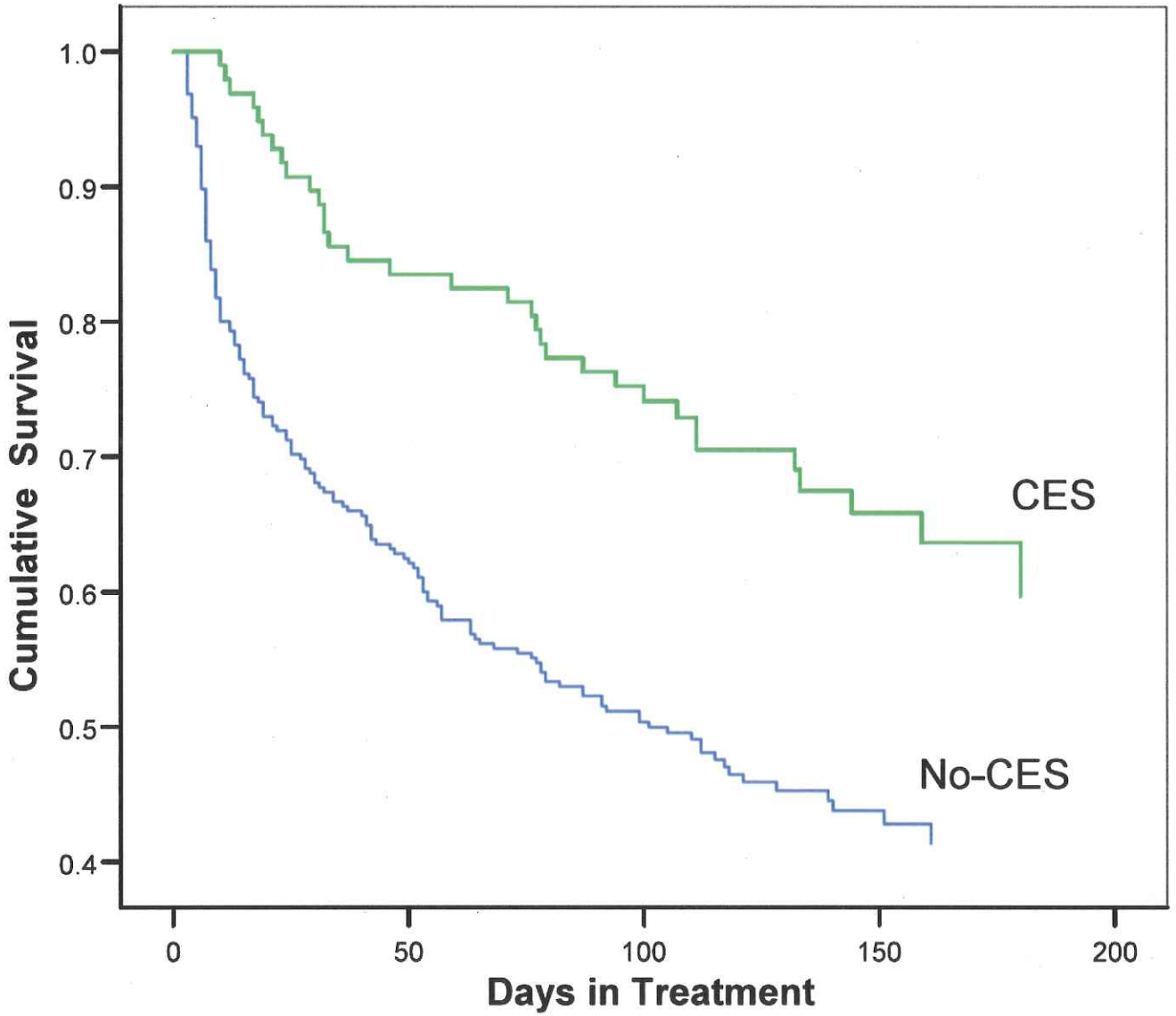



Fig. 1. *Cox regression model (unadjusted) showing treatment retention for clients who participated in CES and clients who did not*

# Patient Feedback

| Client Name | # of Sessions | Client Statement |
|---|---|---|
| Deborah G. | 8 | Client reports improved concentration, sleeping better |
| TimothyC. | 4 | Client reports he starts his day over with the session, it relaxes him |
| Sara R. | 5 | Client reports feeling a little less stressed |
| Maria V. | 5 | Client reports feeling more relaxed, sleeping better, and less anxious |
| Jose V. | 6 | Client reports feeling more relaxed, and less stress |
| Patricia W. | 3 | Client reports Dot having feeling any different |
| Eddar R. | 3 | Client reports less stressed, relaxed |
| Karsheam P. | 4 | Client reports sleeping better, attitude improvement |
| Jason M. | 3 | Client reports getting better sleep |
| Jaclyn T. | 2 | Client reports sleeping better andfeeling better |
| Jon T. | 2 | Client reports sleeping better |
| Jason L. | 3 | Client reports being able to sleep better, and more focused |
| Davon H. | 2 | Client reports feeling more relaxed |
| Orlando M. | 1 | Client reports that he liked the session and wants to continue |

# Cortical Stimulation

## Rescuing cocaine-induced prefrontal cortex hypoactivity prevents compulsive cocaine seeking

Billy T. Chen, Hau-Jie Yau, Christina Hatch, Ikue Kusumoto-Yoshida, Saemi L. Cho, F. Woodward Hopf & Antonello Bonci

*Nature* **496**, 359–362 (18 April 2013) doi:10.1038/nature12024
Received 01 March 2012 | Accepted 18 February 2013 | Published online 03 April 2013

Loss of control over harmful drug seeking is one of the most intractable aspects of addiction, as human substance abusers continue to pursue drugs despite incurring significant negative consequences[1]. Human studies have suggested that deficits in prefrontal cortical function and consequential loss of inhibitory control[2, 3, 4] could be crucial in promoting compulsive drug use. However, it remains unknown whether chronic drug use compromises cortical activity and, equally important, whether this deficit promotes compulsive cocaine seeking. Here we use a rat model of compulsive drug seeking[5, 6, 7, 8] in which cocaine seeking persists in a subgroup of rats despite delivery of noxious foot shocks. We show that prolonged cocaine self-administration decreases *ex vivo* intrinsic excitability of deep-layer pyramidal neurons in the prelimbic cortex, which was significantly more pronounced in compulsive drug-seeking animals. Furthermore, compensating for hypoactive prelimbic cortex neurons with *in vivo* optogenetic prelimbic cortex stimulation significantly prevented compulsive cocaine seeking, whereas optogenetic prelimbic cortex inhibition significantly increased compulsive cocaine seeking. Our results show a marked reduction in prelimbic cortex excitability in compulsive cocaine-seeking rats, and that *in vivo* optogenetic prelimbic cortex stimulation decreased compulsive drug-seeking behaviours. Thus, targeted stimulation of the prefrontal cortex could serve as a promising therapy for treating compulsive drug use.

# ADD/ADHD Studies

- Southwark et al, A Study of the Effects of Cranial Electrotherapy Stimulation on Attention and Concentration, (Family Institute), 1991.

- Richard Brown, Non-Drug Treatments for ADD/ADHD, New Options for Kids, Adults & Clinicians, 2012

- Cranial Electrotherapy Stimulation, A Monograph, Raymond B. Smith, Ph.D.

# Bipolar Depression

## A Single Blind, Randomized, Sham Controlled Study of Cranial Electrical Stimulation in Bipolar II Disorder

SS Koppolu, G Kazariants, M Varvara, D McClure, Z Yaseen, AMR Lee, I Galynker
Beth Israel Medical Center, New York, NY

## Abstract

**Introduction:** Cranial Electrical Stimulation (CES) is a non-invasive brain stimulation technology which has been FDA cleared for the treatment of depression, anxiety and insomnia. However, there have not been any clinical trials evaluating its efficacy in treating the depressive phase of bipolar II disorder. This single blind, randomized, sham controlled study examines the safety and efficacy in this particular group of patients. Preliminary results of the study are discussed.

**Methods:** Eight patients diagnosed with bipolar II disorder currently experiencing depression symptoms by SCID-P were recruited from the Family Center for Bipolar in New York City. Subjects were randomly assigned to two groups in phase I: an active treatment group (n=4) and a sham to active treatment crossover group (control group) (n=4), for the first two weeks of daily 20 minute treatment sessions. Following this, both groups received an open-label active treatment for an additional two weeks in phase II. Depression symptoms were rated using the Hamilton Depression Rating Scale (HAM-D), the Beck Depression Inventory (BDI) and the quality of life was assessed using the Quality of Life Satisfaction and Enjoyment Questionnaire (Q-LES-Q). The assessments were completed at the study intake, at the end of the 2nd week (after a period of active or sham treatment) and at the end of the 4th week (after an additional two weeks of open-label active treatment for both groups).

**Results:** Patients were 62.5% male and 62.5% white, with a mean age of 50.10. The treatment group had a 32% decrease on the HAM-D mean score (baseline M=20.25, 4th week M=13.67), also a 32% decrease on the BDI mean score (baseline M=36.25, 4th week M=24.50) and a minimal change on the Q-LES-Q (baseline M=30.40, 4th week M=31.50). The control group after a period of sham treatment had 18% decrease on the HAM-D mean score (baseline M=19.50, 2nd week M=16.00), a 7% decrease on the BDI mean score (baseline M=34.00, the 2nd week M=31.50.) After an additional two weeks of active treatment the control group had a 33% decrease on the HAM-D (M=10.67), a 41% decrease on the BDI (M=18.67) and a 124% increase on the Q-LES-Q (M=42.00) compared with the scores at the end of the 2nd week.

**Discussion:** CES therapy had a positive treatment effect reducing the level of depression in the experimental group from severe to mild. In the control group the depression level decreased mildly on the clinician administered scale and the self-report scale after the period of sham treatment . After an additional two weeks of open-label active treatment the control group also had a substantial reduction in depression symptom levels and marked increase in the level of life satisfaction.

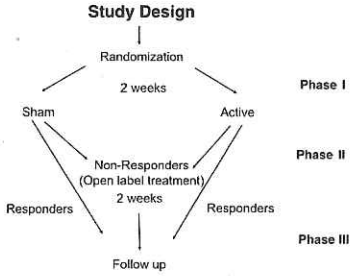
The research was funded by the Fisher-Wallace Laboratories.

## Introduction

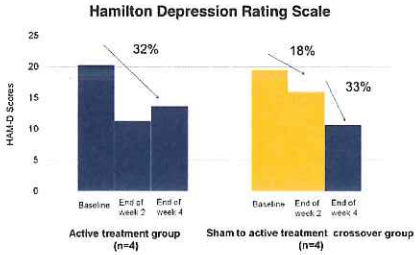
- Cranial Electrical Stimulation (CES) is a non-invasive brain stimulation technology which has been FDA cleared for the treatment of depression, anxiety and insomnia.
- However, there have not been any clinical trials evaluating its efficacy in treating the depressive phase of bipolar II disorder.
- This study examines the safety and efficacy in this particular group of patients.
- Cranial Electrical Stimulation (CES) uses a small (1-2 mA) alternating current (5 Hz – 15,000 Hz) and it has been widely used in Europe since 1950 and United States since the 1960's.

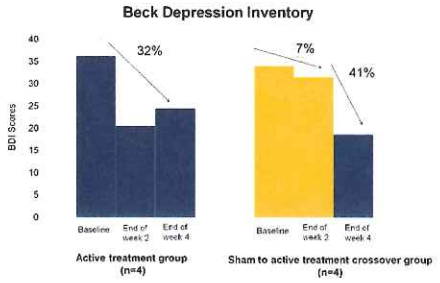
## Methods

- Inclusion criteria: diagnosis of bipolar II disorder currently in the depressive phase by SCID-P.
- Exclusion criteria: non bipolar II psychiatric diagnosis, significant current autoimmune or endocrine disorder affecting the brain, unstable cardiac disease, current active suicidal plan, history of seizures or epilepsy, skull fractures, deep brain stimulation, subject has a pacemaker or is pregnant.
- Sixty eight people were phone screened, however, the majority failed to meet the inclusion criteria for various reasons (such as a mixed episode, history of seizures or epilepsy, active suicidal ideation with a plan, pregnancy, and others.) From the pre-qualified set, eleven were invited for the initial assessment and eight candidates were enrolled in the study.
- Active treatment group received an active treatment during the first two weeks under the blinded conditions following by an open-label active treatment for the next two weeks.
- Sham to active treatment crossover group received sham treatment during the first two weeks under the blinded conditions following by an open-label active treatment for the next two weeks.
- Outcome measures:
  - Hamilton Depression Rating Scale (HAM-D)
  - Beck Depression Inventory (BDI)
  - Quality of Life Enjoyment and Satisfaction Questionnaire (QLES-Q)




## Results




**Demographic characteristics**

| Characteristic | Active treatment group (N=4) M (SD) | Control group (N=4) M (SD) |
|---|---|---|
| Age | 48.8 (14.32) | 51.5 (19.43) |
| Years of Education | 15.8 (2.36) | 18.8 (1.71) |
| | n (%) | n (%) |
| Sex | | |
| Male | 3 (75) | 2 (50) |
| Race | | |
| Black | 1 (25) | 1 (25) |
| White | 3 (75) | 2 (50) |
| Other | 0 (0) | 1 (25) |
| Job/School Status | | |
| Retired | 1 (25) | 1 (25) |
| Unable to work | 0 (0) | 1 (25) |
| Unemployed and worked in the past | 1 (25) | 1 (25) |
| School/college part time | 1 (25) | 0 (0) |
| Part time job | | 1 (25) |

- The groups were statistically different on the level of quality of life after the randomized treatment period ($p$=0.049), experimental group reporting a higher level of life satisfaction than the control group.
- Both groups also differed significantly on the level of clinician rated global clinical improvement of illness after the randomized treatment period ($p$=0.030), experimental group improving and control group not changing .
- The scores for both groups followed in the same direction on all the other scales, however not reaching statistically significant difference because of the small sample size.

## Discussion

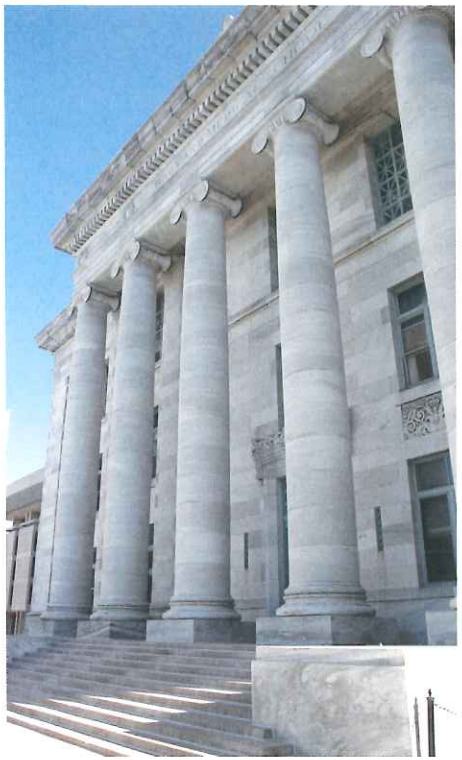
- CES therapy had a positive treatment effect reducing the level of depression in the experimental group from severe to mild and was associated with an increase in quality of life during the treatment period.
- In the sham to active treatment crossover group the depression level decreased slightly after the sham treatment period.
- After an additional two weeks of open-label active treatment the sham to active treatment crossover group also had a marked reduction in depression symptoms levels and a significant increase in the level of life enjoyment and satisfaction.

## References

Shealy, C., & Thomlinson, P. (2008). Safe effective nondrug treatment of chronic depression: A review of research on low-voltage cranial electrical stimulation and other adjunctive therapies. *Complementary Health Practice Review, 13*(2), 92-99. doi:10.1177/1533210108317232

Manning, J. (2003). Difficult-to-treat depressions: A primary care perspective. *Journal Of Clinical Psychiatry, 64*(Suupl1), 24-31.

# Ongoing Research



McLean Hospital (Harvard) – PTSD

MGH – Major Depressive Disorder

Beth Israel Medical Center – Bipolar Disorder

NYU / University of Chicago – TBI

# Additional Information

**www.FisherWallace.com**

**Chip Fisher, President**

chip@fisherwallace.com