Efficacy of neurofeedback for executive and memory function in dementia

Marvin H. Berman, Ph.D., Principal Investigator Jon Frederick, Ph.D., Project Director

QuietMIND FOUNDATION
www.quietmindfdn.org

Abstract

Background
Previous studies have shown that dementia is associated with quantitative EEG (QEEG) abnormalities including increased slow activity and a reduction in the dominant alpha frequency.

Objective
This study tested whether using EEG biofeedback (neurofeedback) training to normalize abnormal EEG activity could improve measures of memory and executive function.

Methods
Participants were randomly assigned to immediate treatment or to a waiting-list control group. All participants received neuropsychological and QEEG assessments before and after treatment or control conditions. Each participant's pre-treatment QEEG was compared to a normative database, and neurofeedback protocols were customized to normalize EEG activity at significantly deviant (>1.0±SD) frequencies and specific scalp locations. Treatment consisted of 30 or 40, 30-minute neurofeedback training sessions involving operant conditioning of the EEG using simultaneous visual, auditory, and tactile reinforcements. To date, 16 subjects and 11 waitlist controls have completed treatment.

Results
Pre- and posttreatment scores displayed significant improvements in verbal memory (mean Mini Mental Status Exam [MMSE] orientation and recall, Memory Assessment Scales' (MAS) list and prose memory, $p < .05$); visual memory (mean MAS Visual and Rey Figure recall, $p < .05$); Behavioral Rating Inventory of Executive Function (mean self and informant General Executive Composite, $p < .05$); Immediate Visual and Auditory (IVA) continuous performance test response control ($p < .05$). Trends toward improvement were seen in the MMSE ($p = .072$) and psychiatric distress measured by the Symptom Checklist 90-Revised ($p = .085$). A number of executive function measures did not significantly improve, including the IVA Attention, Wisconsin Card Sort, and Delis-Kaplan Executive Function System (with the exception of verbal fluency, $p < .05$). In the treatment group, the standardized mean treatment effect on variables that improved (at $p < .10$) correlated significantly with the pretreatment MAS Global Memory index ($r = .71$, $p < .01$). In the control group, this correlation was -.06.

Conclusion
These results support QEEG-based neurofeedback training as a "possibly efficacious" treatment for dementia. The strong correlation of efficacy with pretreatment memory suggests the importance of learning and memory in this treatment's mechanism of action, and suggests that neurofeedback is more strongly indicated as an earlier stage intervention.

Introduction

Dementia is associated with a diversity of EEG abnormalities, including increased power in delta (1-3.5 Hz) and theta (4-7 Hz) bands, decreased power in the alpha (8-12 Hz) and beta (13-30 Hz) bands (Jackson & Snyder, 2008), and a reduction in the peak alpha frequency (Passant et al., 2005, Chan et al., 2004).

In EEG biofeedback (neurofeedback), an individual's real-time EEG is presented continuously as a visual or auditory signal, and desired variations are rewarded. A standard practice in neurofeedback is to analyze a baseline quantitative EEG (QEEG) during an initial assessment, and build custom neurofeedback protocols designed to reward the normalization of each client's individual abnormalities (Lubar, 2004). Neurofeedback has been shown to be Possibly Efficacious for posttraumatic stress disorder (effective in one study with waiting list controls; Chambless and Holon, 1998); Efficacious for Attention Deficit Hyperactivity Disorder (two or more studies; Monastra, 2005) and Substance Abuse Disorders (Nelson, 2003), and Efficacious and Specific for Seizure Disorders (two or more studies with placebo controls; Nelson, 2003).

A recent double-blind controlled study (Angelakis et al., 2007) showed that neurofeedback training that rewarded increases in the dominant alpha frequency improved cognitive processing speed and executive function in a small sample of normal elderly adults. The present study measures whether neurofeedback provides similar benefits to adults with mild to moderate dementia.

Methods

The following criteria were required for inclusion in the study: (1) a diagnosis of dementia by a physician or clinical psychologist; (2) MMSE >/=20; (3) independence or minimal assistance in activities of daily living; (4) age < 80; (5) BRIEF-A >90th percentile. Exclusion criteria included psychosis, a history of seizures, drug dependence, or greater than moderate dementia.

Measures of psychological function included:
(1) Behavior Rating Inventory of Executive Function-Adult Version (BRIEF-A; self and informant report).
(2) Symptom Checklist 90-R.
(3) Williams' Memory Assessment Scale, (PAR Inc).
(4) Rey-Osterreith Complex Figure Task.
(5) Wisconsin Card Sort Test.
(6) Integrated Visual and Auditory Continuous Performance Test (IVA).
(7) Delis-Kaplan Executive Function Battery (omitting Proverbs, the second Card Sort set, and the Tower test).

A 19-channel referential EEG was recorded using a Mitsar amplifier. Five-minute eyes-open and eyes-closed recordings were compared to a normative database using Neuroguide (Applied Neuroscience, Inc.). Neurofeedback protocols were customized based on the specific frequencies and locations identified as abnormal in each individual. Generally, rewards were provided for decreased 0-8 Hz and 22-35 Hz and increased 10-18 Hz amplitude.

Participants were randomly assigned to either an immediate treatment or waiting list group. Sixteen completed treatment and 12 completed the waiting period. The waiting period was determined by the average treatment completion time. Treatment consisted of 30 or 40 sessions of EEG biofeedback using a Pendant EEG and Bioexplorer software. Desired patterns in the EEG were rewarded by the presentation of a DVD movie. When the EEG varied outside of the desired range, reinforcement was withdrawn by reducing the brightness and volume to 15%.

Psychological and EEG measures were repeated upon completion of treatment or the waiting period.

Results

To optimize statistical power in this small sample, individual test scores were standardized to the sample mean and standard deviation and averaged into categories, as shown in Table 1. Changes in individual test scores are illustrated in figures 1, 2, and 3.

Table 1. One tailed t-test comparisons of pre- and posttreatment effect (standard score differences) vs controls.

Aggregate Variable	Variable Description	Tx	Control	*P*
Executive	IVA, BRIEFA, DKEFS, MAS clustering, WCST, MMSE att/calc	3.72	1.66	0.140
Global Memory	MMSE orientation and recall, MAS Verbal and MAS Visual	4.45	-2.70	0.009
MAS Global Memory	MAS Verbal + MAS Visual	4.17	-1.13	0.045
Verbal Memory	MMSE orientation and recall, MAS list and prose	2.81	-3.69	0.024
Visual Memory	MAS Visual and Rey Figure	6.36	-0.51	0.014

When the differences in the mean standard score of all tests were analyzed, 6/16 participants in the treatment group showed negligible improvement or a decline, compared to 10/12 in the control group. To determine whether some factors made some participants better candidates for neurofeedback than others, pretreatment scores were correlated with the standardized mean treatment effect on variables that improved (at $p < .10$). Among 45 variables considered, the only significant correlations (at $p < .01$) were with MAS Verbal Memory ($r = .632$), Global Memory ($r = .635$), and MAS Global Memory ($r = .714$). However, when Fisher Z-transforms were compared to the control group, only MAS global memory was significantly different ($p < .01$).

Improvement was predicted by 8-18 Hz amplitude in the pretreatment QEEG baselines, but this correlation was not significantly greater than that seen in controls. However, when the average pre-post amplitude differences were compared by t-test, the treated group showed significantly greater amplitude changes in all frequencies higher than 10 Hz (figure 4).

Improvement was also related to a reduction in 1-4 Hz amplitude between pre- and posttreatment eyes-closed QEEG at most locations. This correlation was significantly greater than controls at F4 and C4. This difference is illustrated in figure 5, comparing the average amplitude maps for those who improved most and least in each group.

Discussion

This study showed that neurofeedback training resulted in significant improvement in memory and some aspects of executive function, compared to a waiting list control, suggesting that neurofeedback is a "possibly efficacious" treatment for dementia. The finding that the efficacy of neurofeedback is greater in persons with more intact memory function suggests that this intervention is more strongly indicated for earlier stage cases. It also suggests that learning and memory are involved in neurofeedback's mechanism of action.

While eyes-closed EEG baselines did not predict the efficacy of this treatment, improvement correlated with lower 1-4 Hz amplitudes more in trained participants than in controls, and training resulted in significantly higher amplitudes above 10 Hz. These observations may support the view that neurofeedback works by normalizing abnormal brain rhythms in the direction of training.
The eyes-open QEEGs and the session recordings, not yet analyzed, may provide concurrent validation of these results.
The low subject number in this study made many significant findings borderline and many promising trends undetectable.

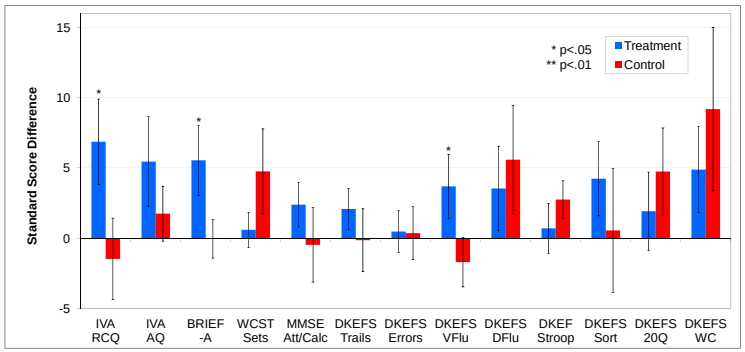

Figure 1. Changes in executive function in treated participants vs controls.

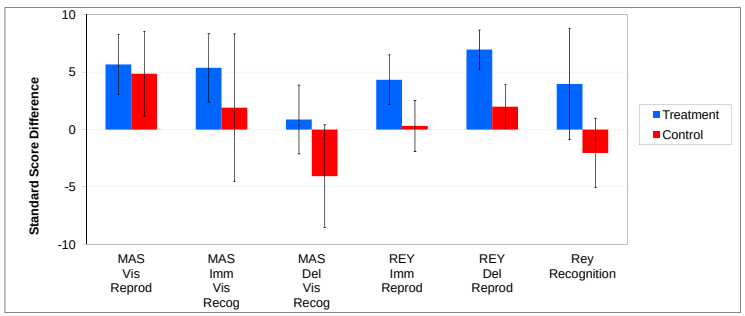

Figure 2. Changes in visual memory in treated participants vs controls.

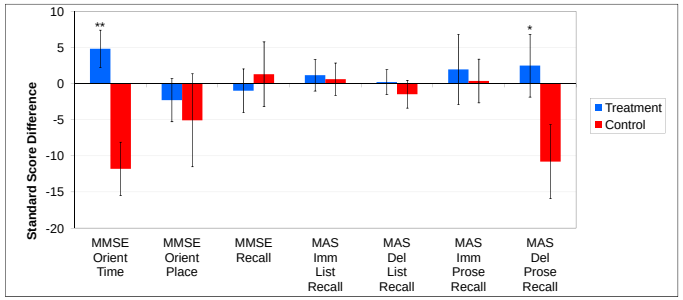

Figure 3. Changes in verbal memory in treated participants vs controls.

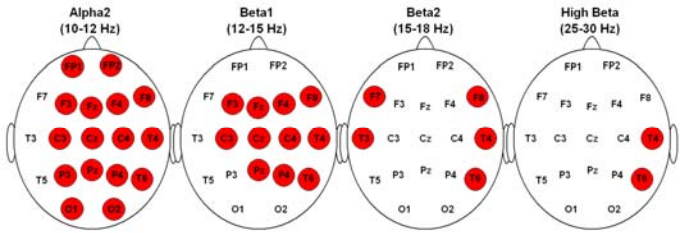

Figure 4. Compared to controls, treated participants showed greater changes in EEG amplitude above 10 Hz in the eyes-closed baselines (red circles denote positive p<.05).

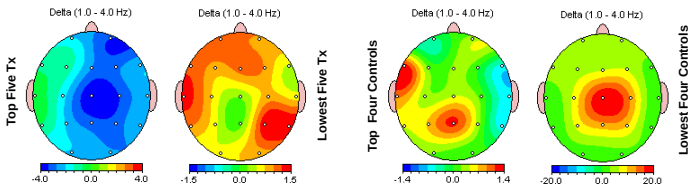

Figure 5. Compared to controls, improvement in treated subjects showed a significantly greater correlation with reduction in slow wave activity.

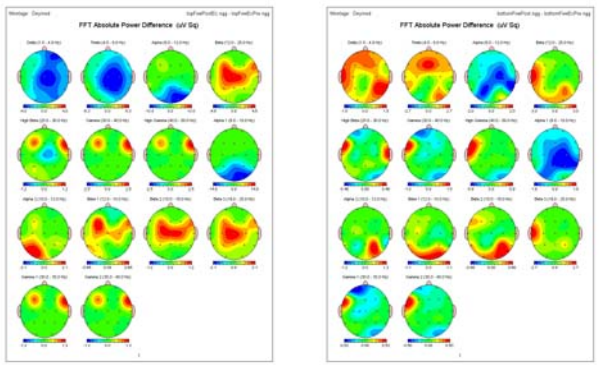

Figure 6. Composite postest-pretest QEEG differences of 5 most and least improved subjects.