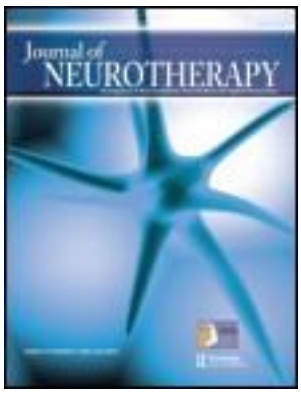

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The Effect of Neurofeedback and Cranial Electrotherapy on Immune Function Within a Group of HIV+ Subjects: A Controlled Study

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SCIENTIFIC FEATURES

THE EFFECT OF NEUROFEEDBACK AND CRANIAL ELECTROTHERAPY ON IMMUNE FUNCTION WITHIN A GROUP OF HIV+ SUBJECTS: A CONTROLLED STUDY

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This study investigated the effects of neurofeedback and cranial electrotherapy on a group of subjects (n = 40) with the human immunodeficiency virus (HIV) over a 16-week period. Subjects were randomly assigned to one of four groups: neurofeedback only (n = 10), cranial electrotherapy only (n = 10), combined neurofeedback and cranial electrotherapy (n = 10), and a waitlist control group (n = 10). After 16-weeks, CD4 counts were significantly greater than controls for the neurofeedback group and combined group. There was no significant change in CD4 count for the cranial electrotherapy group. Results of this pilot study suggest that neurofeedback may improve immune function and warrants further investigation.

INTRODUCTION

Knowledge that the Human Immunodeficiency Virus (HIV) targets and incapacitates the immune system, our primary defense against disease, compelled efforts to find a way to manage the pathogen. Today, 30 years after the identification of HIV, medications have made infection by HIV a chronic manageable disease in the United States; however, there remains no cure. By the end of 2010, the World Health Organization stated that there were 34 million people infected with HIV worldwide; that year alone, 2.7 million people became newly infected, and 1.8 million died from HIV-related diseases.

HIV infection reduces the presence of an important immune modulator, a glycoprotein called the CD4 helper cell. CD4 helper cells are necessary in the initiation of a competent immune response when any potentially lethal matter invades the body. CD4 cells are necessary to amplify the T-cell's ability to coordinate the entire immune system's response. After combining with CD4 cells, the T-cells are then able to carry out a variety of the primary functions of the immune system. Some T-cells are involved in the production of antibodies; others identify, surround, destroy, and eliminate invading pathogens including HIV and other common infections. Thus, infection by HIV decreases the absolute number of CD4 helper cells available, which effectively down-regulates the ability of the immune system to fight disease. The absolute CD4 count is part of the routine blood work of HIV infected patients and is used as a measure of immune health as well as a primary factor in determining a patient's prognosis for survival (A. H. Miller, 2010; Turner, Markson, & Taroni, 1996).

The knowledge that the HIV virus first infects, then disables, and ultimately destroys key elements of the human immune system leaving its host unable to fight opportunistic infections quickly focused scientific efforts to understand and control the spread of this pathogen (Cohen, 1993). Fear of the contagion made funding available to research any intervention that offered hope for the containment

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of the virus. This facilitated a willingness to investigate complementary and alternative therapies to improve the capacity of the immune system and to treat the symptoms of infection (Duggan, Peterson, Schutz, Khuder, & Charkraborty, 2001).

Concomitantly with the investment of resources to determine a medical solution to HIV in the early 1980s, scientists were investigating a myriad of related phenomenon, and some important theories were converging. For example, Piaget, who was studying stages of cognitive development in children, and Darwin, who studied evolution, described inherently greater plasticity in humans, both in our genetic heritage and in an individual's potential during development. This caused a minor paradigm shift away from the 16th-century mind–body dualistic tradition upon which Western medicine had evolved. Scientists began taking a broader, more systems view of adaptation via assimilation and accommodation. With regard to developments in neuroscience, the capacity of the brain to change in response to experience was emerging as critical feature of brain development honed by natural selection. The awareness that the brain is dynamically impacted by both exogenous and endogenous events led to studies proving that stress was a factor modulating immunological health (Sommershof et al., 2009). By the late 1980s, physicians and mental health clinicians considered their patient's emotional state to be a major cofactor in the health of their patients.

The central nervous system (CNS) affects immunity through extensive bidirectional neuronal and neuroendocrine connections (Besedofsky et al., 1983; Black, 1994; Darjik & Berkenbosch, 1991; Felten & Felten, 1991). Although research shows that brain dysregulation occurs early after HIV infection (Baldeweg et al., 1997), studies also demonstrate that the CNS can be conditioned to suppress (Bvobjerg, Redd, Maier, & Hollard 1990; Klosterhalfen & Klosterhalfen, 1983) or enhance (Solvason, Ghanta, & Hiramoto, 1988) elements of immune function. Because emotions modulate the production of neuropeptides and neurotransmitters, they also influence the immune system's response to invading pathogens. Although some investigators found that relaxation improved mood, these studies failed show a positive correlation with CD4 count in HIV+ subjects (Aurbach, Oleson, & Sloman, 1992; Lutgendorf et al., 1997). Other studies, however, have shown consistently positive correlations between the suppression of immune function and a depressed mood (V. Miller et al., 1999). In one study, CD4+ T lymphocytes increased in individuals who enrolled in stress reduction programs (Creswell, Myers, Cole, & Irwin, 2009). As a result, we chose to include measures from the Symptom Checklist (SCL-90) and a stress inventory form in the current study to track correlations between emotional states and changes in CD4 counts.

Biofeedback training has a positive impact on a variety of symptoms not previously thought to be controllable (Andreychuk & Shriver, 1975). The physiological signal utilized by neurofeedback is the electroencephalogram (EEG), which is shaped by the feedback to guide it toward better functioning. The EEG reflects the summed rhythmic discharges from projections of thalamic nuclei (Striade, McCormick, & Sejnowski, 1993) and has utility as an indicator of normal states of consciousness as well as identifying localized and generalized brain pathology. Studies dating back to 1969 indicate that the frequency and topography of human EEG respond to operant conditioning by neurofeedback training, which alters the incidence, magnitude, and organization of neuronal oscillations (De Pascalis & Silveri, 1986; Sterman, 1996). Neurofeedback training is an accepted intervention, demonstrating efficacy with regard to treating certain disorders by improving CNS function (Tozzo, Elfner, & May, 1988).

The effects of neurofeedback on the immune system have been investigated from both a theoretical and experimental standpoint (Auerbach et al., 1992; Schummer, 1996). Auerbach et al. studied the effects of thermal biofeedback on a group of HIV+subjects and found the group showed improvement in a variety of symptoms, but there was no report of changes in CD4 count. Because neurofeedback training impacts brain function at the neuronal level, it has been hypothesized that neurofeedback

training would directly modulate the extensive bidirectional neuronal connections and feedback loops in and between the CNS and immune system (Schummer, 1996). Because there is an extensive body of evidence showing that alpha or alpha-theta neurofeedback training enhances mood, it is reasonable to suggest there might be an increase in CD4 count in subjects undergoing this particular treatment. As the amplitude in the alpha (8–12 Hz) and theta (4–8 Hz) frequency bands increase in the human EEG, a subject reports less tension, lower levels of anxiety, and occasional drowsiness. Thus, alpha and theta were the frequencies chosen for the neurofeedback protocol in the present study.

Cranial electrical stimulation (CES) is another alternative treatment that is often compared to neurofeedback training. CES protocols use a small, pulsed electric current across the head every day for about 15 to 30 min. Those who manufacture and use this treatment claim they experience benefits such as lowered stress levels and improved sleep. Others claim it decreased symptoms associated with anxiety and depression. Although its use remains experimental, we chose to include this as a treatment condition to see what effects CES may have on our dependent variables.

For the present study, we predicted neurofeedback and cranial electrotherapy would significantly reduce HIV-related symptoms compared to the control group. In addition, we hypothesized that neurofeedback and cranial electrotherapy would significantly reduce subjective measures of stress compared to the control group. We also predicted an increase of CD4+ cell counts in HIV-infected individuals compared to the control group with neurofeedback and cranial electrotherapy.

METHODS

Subjects

HIV+ volunteers without overt AIDS were recruited from the community (Hollywood, CA). Selection criteria were set as 18 to 55 years of age with a total of total CD4+ counts from 150 to 650/cc (lab normal 400 to 1,770). All subjects were interviewed to ensure qualifications for the study. Subjects with overt depression or other Axis I diagnoses and those using illicit drugs or alcohol were excluded from the study. The study was privately funded and was not reviewed by an Institutional Review Board. Volunteers did, however, complete informed consent forms prior to their participation.

Procedure

After informed consent was obtained, participants were given the Symptom Checklist (SCL-90-R, Version 1.0, 1990 revision, Derogatis) to fill out every week of study. The checklist scored symptoms such as fever, fatigue, pain, nausea, and insomnia. At initiation and at 2 and 4 months, complete blood counts including total lymphocyte count and serum chemistry were measured. Concomitantly, absolute CD4+ and CD8+ counts were measured as previously described (Flaherty, Wagner, Gross, & Panyik, 1997; Consolidated Lab Services, Van Nuys, CA) on samples collected during morning attendance at the clinic. CD4+ and CD8+ cells were counted on blood (50 μL) incubated for 15 min at room temperature in the dark with 20 μL color-tagged monoclonal antibodies (Becton Dickinson, San Jose, CA). Red blood cells were lysed, and remnant cells were washed and assayed by a fluorescence-activated cell sorter (Becton Dickinson True Count Method).

Patients were randomly divided into four groups ($n = 10$/group): (a) in office, EEG alpha neurofeedback; (b) at home daily cranial electrotherapy; (c) both in office neurofeedback and home electrotherapy; and (d) waitlist control. Participants in the neurofeedback treatment condition were given neurofeedback therapy for 20 min twice weekly for 16 weeks under the guidance of a randomly selected investigator who continued with that subject throughout training. Individuals in the cranial electrotherapy group were trained to use the product and asked to train at home every day for 20 min. The combined therapy group was given the EEG neurofeedback training for the same weekly time (twice/week) as well as daily cranial electrotherapy.

Subjects in the waitlist control group were interviewed weekly and continued with usual

therapy with no other intervention. All subjects continued on their usual medical therapies and were not informed of any results until completion of the study. A one-way analysis of variance was used to test for overall difference among groups for each dependent variable. This was followed by pairwise comparisons between groups using a (post hoc) Dunnett's *t* test.

EEG Biofeedback Treatment Protocol

EEG neurofeedback was performed using linked ears (reference and ground) with the active electrode at Oz (occipital midline according to the International 10–20 system, Cap Scan, New York, NY). Fast Fourier Transform using a Cooley-Tukey algorithm was applied to each 2.56-s epoch, and the square root of the absolute power coefficients was computed for each epoch. Subjects were rewarded by a tone when alpha amplitude (8–12 Hz) exceeded their initial testing amplitude (30 s with eyes closed). Drifting into sleep was actively prevented by constantly monitoring the EEG activity of subjects during neurofeedback. If EEG deteriorated into sleep, the assigned investigator would tell the subject to refocus on the tone. When subjects could sustain alpha amplitude at double the baseline level for 20 minutes, the reward tone was shifted to a slightly lower frequency (i.e., low alpha-theta, 6–8 Hz); training was continued for a total of 16 weeks. Training did not reward slower (i.e., theta, 4-6 Hz) frequencies, which instead of quiet attention indicate potential pathology or patterns of extreme drowsiness (Johnson, Seales, Naitoh, Church, & Sinclair, 1979). To minimize placebo bias (Cott, Pavloski, & Goldman, 1981), subjects were not informed of subjective or immune benefits they might derive from training.

Cranial Electrotherapy Treatment Protocol

Cranial electrotherapy was conducted using an electrical stimulating device (''electrotherapy'') believed by its proponents to induce alpha by application of oscillating 10 Hz, 200 μamp currents applied to both ears (Alpha-Stim Model 2000 GL, Hollywood, CA, Smith/Shiromoto; Brotman, 1989; Wilson & Childs, 1998). The intensity of the electrical current did not allow verification of actual EEG amplitude changes caused by the applied signal.

RESULTS

At baseline, there were no group differences in CD4 cell count ($p = .72$). All subjects completed the entire 16 weeks of study and the entire symptom questionnaire on each occasion by previously defined rules. All subjects who received EEG neurofeedback with or without electrotherapy could sustain criterion alpha amplitude for 20 min by completion of the study. The average time for transition from mid-alpha frequency to low alpha was 10 weeks with a range of 6 to 14 weeks. No subject demonstrated increased amplitude of delta frequencies. EEG significantly differed between subjects before and after neurofeedback training. Because results were intended to evaluate responses to particular treatments and not relevance to EEG changes, EEG measures were not performed in control subjects or those who received only electrotherapy. There is no a priori reason to have expected that alpha amplitude would change during the course of the study for control subjects, none of whom developed overt neurological signs during the study.

Subjects receiving EEG neurofeedback reported fewer symptoms (Table 1), clearer mind, less physical pain, less subjective stress, and increased energy. The score on the Symptom Checklist decreased after neurofeedback alone and neurofeedback plus electrotherapy (see Table 1; $p < .01$) in comparison to the control groups. Results did not significantly differ from control subjects for those who received electrotherapy alone ($p = .29$).

Baseline total CD4+ lymphocyte counts did not differ between groups ($p = .72$). After 16 weeks, CD4+ counts were significantly higher in the neurofeedback ($p < .02$) and combined neurofeedback/electrotherapy ($p < .05$) groups (see Figure 1). Changes in CD4+ counts were significant at 8 weeks for those who

TABLE 1. Average Group Symptom Checklist-90-R (SCL-90-R) Scores Throughout the 15-Week Training Period

Group	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Control	74	78	81	99	110	93	82	86	90	90	86	73	93	86	
Alpha Stim	55	47	62	47	86	81	74	75	77	71	71	66	59	73	55
Neurofeedback	42	40	35	31	33	29	23	23	23	28	23	24	21	21	29
Combined	42	35	38	30	30	25	23	24	22	21	24	25	25	21	17

Note. Results are shown for the average scores received between groups on the SCL-90-R diagnostic questionnaire. This test, distributed by the Pearson Assessment and Information group, consists of 90 items that correlate with the measure of psychological distress in each subject.

received EEG neurofeedback training plus electrotherapy ($p < .01$) and neurofeedback alone ($p < .01$). During EEG neurofeedback training, CD4+ levels significantly increased between Weeks 8 and 16 ($p < .01$), but no significant change occurred from Weeks 8 to 16 for subjects who received both neurofeedback training and electrotherapy ($p = .47$). Similar results at 16 weeks were found for total CD4+ counts, for the ratio of CD4+ to CD8+ cells, and for CD4+ cells expressed as a percentage of total lymphocytes (Table 2). No significant change occurred in total lymphocyte count. No significant change in CD4+ counts was noted after electrotherapy alone or control conditions at 8 and 16 weeks ($p = .5$), but there was a significant increase from 8 to 16 weeks after electrotherapy alone ($p < .05$). Because there was no statistical difference between the neurofeedback and combined groups at the 2- and 4-month time points, we dismissed the possibility of an interaction between neurofeedback and cranial electrotherapy during combined therapy.

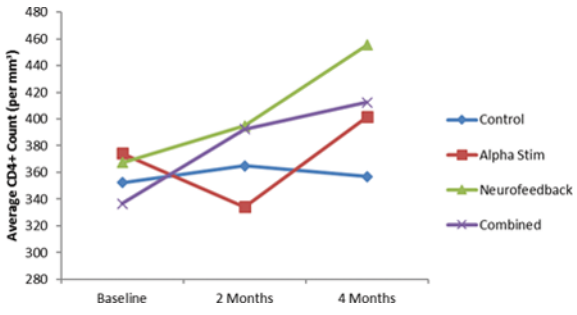

FIGURE 1. Average CD4+ T lymphocyte counts per cubic millimeter in each group at baseline, two months, and four months. *Note*. CD4 levels were measured via blood withdrawals in all subjects during major time points of the study. CD4+ T lymphocyte count is the primary indicator of HIV disease progression. (Color figure available online.)

DISCUSSION

This study has shown that neurofeedback may be an effective tool in the treatment of CD4 counts. Furthermore, these effects were not seen in those subjects who received cranial electrotherapy, consistent with that fact that the neurofeedback and combined groups did not show significant differences. Patients with symptomatic HIV infection were able to train with alpha neurofeedback to enhance amplitude of alpha rhythms. This training improved symptoms of stress and illness, and absolute CD4+ counts were also increased. Symptoms were not improved in the waitlist control group. There was a significant increase of CD4+ counts within 2 months of electrotherapy and neurofeedback combined that persisted for the remaining 2 months of training. With neurofeedback alone, there was a nonsignificant trend to increased CD4+ counts after 2 months of training even though symptoms and stress had improved significantly within 2 months. By 4 months, the improvement of CD4+ counts reached statistical significance. The increased significance over time supports a true shift toward increased production of CD4+ cells and not merely demargination. Electrotherapy is reported to improve mood (Smith & Shiromoto, 1992), improve attention (Brotman, 1989; Madden & Kirsche, 1987; Wilson & Childs, 1988), and decrease fear responses by way of the limbic system (Dymond, Coger, & Serafetinides, 1975). This method led to a time-wise trend to increase CD4+ counts, but results were not significantly higher than baseline after 16 weeks in the current studies. Stress inventory and symptom checklist scores tended to be lower

TABLE 2. Raw CD4+ Lymphocyte Data for All Subjects

Subject	Baseline	2 months	4 months	2 months – baseline	4 months – 2 months	4 months – baseline	% change over 4 months
C1	556	561	679	5	118	123	22.12%
C2	310	390	316	80	−74	6	1.94%
C3	284	449	358	165	−91	74	26.06%
C4	310	300	323	−10	23	13	4.19%
C5	250	270	220	20	−50	−30	−12.00%
C6	171	114	116	−57	2	−55	−32.16%
C7	432	422	395	−10	−27	−37	−8.56%
C8	454	439	507	−15	68	53	11.67%
C9	422	390	306	−32	−84	−116	−27.49%
C10	335	315	350	−20	35	15	4.48%
AS1	540	286	470	−254	184	−70	−12.96%
AS2	339	369	329	30	−40	−10	−2.95%
AS3	422	395	539	−27	144	117	27.73%
AS4	212	269	320	57	51	108	50.94%
AS5	320	220	360	−100	140	40	12.50%
AS6	266	217	287	−49	70	21	7.89%
AS7	189	171	116	−18	−55	−73	−38.62%
AS8	454	439	507	−15	68	53	11.67%
AS9	556	561	553	5	−8	−3	−0.54%
AS10	444	415	533	−29	118	89	20.05%
N1	205	340	423	135	83	218	106.34%
N2	426	449	586	23	137	160	37.56%
N3	540	550	510	10	−40	−30	−5.56%
N4	194	217	281	23	64	87	44.85%
N5	240	157	239	−83	82	−1	−0.42%
N6	410	461	478	51	17	68	16.59%
N7	223	274	324	51	50	101	45.29%
N8	640	687	722	47	35	82	12.81%
N9	548	559	669	11	110	121	22.08%
N10	248	253	321	5	68	73	29.44%
NAS1	427	574	774	147	200	347	81.26%
NAS2	200	250	270	50	20	70	35.00%
NAS3	260	260	230	0	−30	−30	−11.54%
NAS4	180	267	280	87	13	100	55.56%
NAS5	479	592	679	113	87	200	41.75%
NAS6	365	342	381	−23	39	16	4.38%
NAS7	440	530	570	90	40	130	29.55%
NAS8	180	265	280	85	15	100	55.56%
NAS9	280	265	197	−15	−68	−83	−29.64%
NAS10	554	578	464	24	−114	−90	−16.25%

Note. This data tabulates raw data of CD4+ lymphocyte counts for each individual during the major time points of the experiment during which plasma was extracted and biochemically analyzed (baseline, 2 months, and 4 months). Subjects are named based on the group to which they are assigned: control (C), Alpha-Stim only (AS), neurofeedback only (N), or combined neurofeedback/Alpha-Stim (NAS). The absolute differences of the counts at each assessment point are also shown, as well as the percent change of these values over the 4-month period.

and CD4+ counts tended to be higher after electrotherapy, but this did not reach statistical significance. This supports the impact of neurofeedback compared to electrotherapy, which appears to have acted in the direction of improved symptoms and stress. In comparison, improvement of CD4+ counts was significant and was greater after neurofeedback.

The mechanism(s) of immune benefits was not determined by the current study. One might have expected that neurofeedback training could decrease stress (Hardt & Kamiya, 1978) by promoting relaxation. This was not the usual response of subjects in the current study, many of whom instead reported greater energy and clarity of thoughts. In prior studies

of therapies intended to decrease stress in HIV patients, symptoms improved, but CD4+ counts did not increase (Auerbach et al., 1992; Lutgendorf et al., 1997). The current findings may stem from lower anxiety (Peniston & Kulkokosky, 1991), but this would have been more likely in the most anxious subset (Hardt & Kamiya, 1978), and such subjects were not studied. Electrotherapy is reported to decrease fear perception and depression, but no significant CD4+ benefits from such therapy were found in the current study. Depression is also reported to improve after alpha EEG training (Saxby & Peniston, 1995), yet the exclusion of depressed subjects minimized most effects of this variable in the study. Higher CD4+ counts may have resulted from episodes of rest during neurofeedback, but rest alone for as long as 60 min was reported to *decrease* CD4+ counts (Campbell, Aurelius, Blowes, & Harvey, 1997). So it appears that relaxed mood alone does not explain the benefits observed in the present study. One distinction between relaxation training and EEG neurofeedback is the ongoing (real-time) validation during training by rigorous neurophysiologic criteria. It is not clear whether this element led to greater psychoimmunological responses.

The benefits in the current study may have derived from attention given with verbal instructions from the trainer (Watson & Herder, 1980), but such benefit was not shown in previous studies (Auerbach et al., 1992; Lutgendorf et al., 1997; McCain, Zeller, Cella, Urbanski, & Novak, 1996). It cannot be definitively confirmed that such attention did not lead to these results, but the attention from other measures has not led to such effects. A true ''active'' control measure that mimicked the attention devoted to applying the neurofeedback apparatus might have supported the lack of impact from such investigator attention, but such an experimental mode was not performed in the current studies. Subject prejudice may have caused these experimental differences, but others have shown that expectations and hopes did not differ between HIV patients using conventional and alternative psychotherapy including meditation (Langewitz, Ruttimann, Laifer, Maurer, & Kiss, 1994). Hardiness was reported to be greater in those who sought such alternative therapies (Carson, 1993). This was not likely to have been a factor in the current studies based on the randomized design. Lack of baseline differences between study groups supports absence of selection bias.

It appears that factors such as relief of anxiety, lowered stress, improved depression, and rest or relaxation alone do not explain the benefits found in the current studies. One subject obtained a home device and continued EEG alpha training after completion of study and was able to normalize CD4+ levels (1,400/cc) with no change of antiviral therapy; 2 years later she became asymptomatic and was able to return to full-time work. Although prior publications have not shown the same immune benefits as the current studies, there may be other EEG approaches not yet tested to achieve the same end, including increased coherence (Dillbeck & Vesely, 1986) and enhanced fast frequency sensorimotor rhythms.

EEG changes derive from the dynamics of thalamic relay cell polarization that impact intrinsic oscillation within thalamocortical relay circuits (Striade et al., 1993). Lesion experiments and depot injection studies support localized CNS effects leading to increased alpha power (Schellenburg, Schwarz, Knorr, & Haute, 1992). The protocol used most often in clinical practice, and in the current studies, applies symbolic reinforcement to enhance particular rhythms. There might have been modification in the chain of neuroimmunologic control, but such changes have yet to be verified after neurotherapy.

It is not known how alpha EEG neurofeedback led to improved immune function. Similar shifts in subjective mood can be obtained with either increased or decreased alpha activity (Cott et al., 1981). There may be a threshold for benefit attained by increasing amplitude of low-frequency activity. Such a pattern of enhanced alpha activity may be found in some normal subjects (De Prado, Da Silva, & Lima, 1993) and among regular practitioners of meditation (Delmonte, 1984), but such treatments

have not led to the same benefits as occurred in HIV+ patients after neurofeedback. Low-amplitude activity may indicate brain atrophy (Harden, Daras, Tuchman, & Koppel, 1993), but there were no indications of such diminished alpha amplitude or of organic psychosis in the patients during the current studies. Similarly, markedly high amplitude of slow frequency components, which would have reflected local brain pathology, was not evident. Selective enhancement of alpha amplitude, as in the current studies, related to improved mood, vigor, and immune function.

The neurochemical distinctions were not investigated. Incoming peptidergic signals may be changed with EEG training through altered endopeptidase activity (Fricchoine & Stefano, 1994) and neurotransmitter alternations (Moldofsky, 1989). EEG neurofeedback may cause dendritic sprouting and shift neural programming (Diamond, Johnson, & Ingham, 1975; Scheibel, Conrad, Perdue, Tomiyasu, & Wechsler, 1991; Sterman, 1996), and it is possible that this contributed to immune changes.

It is not clear from the current studies if these results can be expanded to patients with symptomatic disease of the CNS who may likely have increased alpha amplitude. Although higher levels of CD4+ lymphocytes relate to better prognosis for HIV patients, there may be several immunologic roles for such cells. Symptomatic improvements suggest clinical benefit, but the results of these preliminary studies need replication before broader application.

At the time of the study in 1992, Highly Active Antiretroviral Therapy was not widely available to patients suffering from HIV. Therefore, compliance by afflicted individuals was easily attainable as there were very few alternative options. In a way, this contributed to the power of the study because there were fewer confounding factors that could have had a role in the parameters being tested in the study. However, this means that the study may be a bit dated in both the equipment and knowledge advances, which have been developed since this time.

For patients who received cranial electrotherapy, Alpha-Stim units were taken home for self-training. The accountability for daily training compliance was held entirely with the subjects themselves. Because of this, some may criticize that this accountability may not have been properly held in check. However, close surveillance was kept with the subjects through frequent use of questionnaires and phone calls. Also, the study occurred during a time at which there were no effective alternatives to HIV therapies, and thus patients were most likely diligent and compelled to commit to new treatment possibilities.

Future studies should address the efficacy of new neurofeedback protocols in treatment of HIV subjects. The current study used Oz training, which is no longer a frequently trained neurofeedback site. Currently, Pz is more commonly used among clinicians in stress management protocols such as alpha-theta training (Peniston & Kulkokosky, 1991). With our current technology, we can now further quantify the effects of neurofeedback as a therapy by the addition of a sham condition in which a patient receives false reward stimuli during his or her neurofeedback session. This can account for placebo bias that may be occurring during the in-clinic biofeedback process. With the advent of current antiretroviral solutions to HIV infection, it may now be difficult to provide conclusive evidence for the efficacy of neurofeedback by itself. This would require complications in creating control groups, as patients will be less inclined to stop HAART medications for an experimental treatment alternative because these medications are already proven to be effective. Therefore, although dated, the study that we conducted several years ago may be the strongest objective measure of the symptomatic benefits that neurofeedback and cranial electrotherapy provide.

REFERENCES

Andreychuk, T., & Shriver, C. (1975). Hypnosis and biofeedback in the treatment of migraine headache. *International Journal of Clinical and Experimental Hypnosis*, *23*, 172–183.

Auerbach, J. E., Oleson, T. D., & Sloman, G. F. (1992). A behavioral medicine intervention as an adjunctive treatment for HIV related illness. *Psychology & Health*, *6*, 325–334.

Baldeweg, T., Catalan, J., Pugh, K., Gruzelier, J., Lovett, E., Schurlock, H., ... Hawkins, D. (1997). Neurophysiological changes associated with psychiatric symptoms in HIV-infected individuals without AIDS. *Biological Psychiatry*, *41*, 474–487.

Besedovsky, H., del Rey, A., Sorkin, E., Da Prada, M., Burri, R., & Honegger, C. (1983). The immune response evokes changes in brain noradrenergic neurons. *Science*, *221*, 564–566.

Black, P. H. (1994). Immune system–CNS interactions: Effects and immunomodulatory consequences of immune system mediators on the brain. *Antimicrobial Agents and Chemotherapy*, *38*, 1–6.

Brotman, P. (1989). Low-intensity transcranial electrostimulation improves the efficacy of thermal biofeedback and quieting reflex training in the treatment of classical migraine headache. *American Journal of Electromedicine*, *6*, 120–123.

Bvobjerg, D. H., Redd, W. H., Maier, L. A., & Hollard, J. C. (1990). Anticipatory immune suppression and nausea in women receiving cyclic chemotherapy for ovarian cancer. *Journal of Consulting and Clinical Psychology*, *58*, 153.

Campbell, P. J., Aurelius, S., Blowes, G., & Harvey, D. (1997). Decreasing CD4 lymphocyte counts with rest; Implications for the monitoring of HIV infection. *International Journal of STD & AIDS*, *8*, 423–426.

Carson, V. B. (1993). Prayer, meditation, exercise, and special diets: Behaviors of the hardy person with HIV/AIDS. *Journal of the Association of Nurses in AIDS Care*, *4*(3), 18–28.

Cohen, J. (1993). What causes the immune system collapse seen in AIDS? *Science*, *260*, 1256.

Cott, A., Pavloski, R. P., & Goldman, J. A. (1981). Cortical alpha rhythm, biofeedback and the determinants of subjective state. *Journal of Experimental Psychology*, *110*, 381–397.

Creswell, J. D., Myers, H. F., Cole, S. W., & Irwin, M. R. (2009). Mindfulness meditation training effects on CD4+ T lymphocytes in HIV-1 infected adults: A small randomized control trial. *Brain, Behavior, and Immunity*, *23*, 184–188.

Darjik, R., & Berkenbosch, F. (1991). The immune-hypothalamo-pituitary-adrenal axis and autoimmunity. *International Journal of Neuroscience*, *59*, 91–100.

Delmonte, M. M. (1984). Electrocortical activity and related phenomena associated with meditation practice. *International Journal of Neuroscience*, *23*, 217–231.

De Pascalis, V., & Silveri, A. (1986). Effects of feedback control on EEG alpha asymmetry during covert mental tasks. *International Journal of Psychophysiology*, *3*, 163–170.

De Prado, G. F., Da Silva, A. B., & Lima, J. G. (1993). EEG base rhythm in AIDS patients. *Arquivos de Neuro-Psiquiatria*, *51*, 169–174.

Diamond, M. E., Johnson, R. E., & Ingham, C. A. (1975). Morphological changes in the young adult and aging rat cortex, hippocampus and diencephalon. *Behavioral Biology*, *14*, 13–174.

Dillbeck, M. C., & Vesely, S. A. (1986). Participation in the transcendental meditation program and frontal EEG coherence during concept learning. *International Journal of Neuroscience*, *29*, 45–55.

Duggan, J., Peterson, B. S., Schutz, M., Khuder, S., & Charkraborty, J. (2001). Use of complementary and alternative therapies in HIV-infected patients. *AIDS Patient Care and STDs*, *25*, 159–167.

Dymond, A. M., Coger, R. W., & Serafetinides, E. A. (1975). Intracerebral current levels in man during electrosleep therapy. *Biological Psychiatry*, *10*, 101–107.

Felten, S. Y., & Felten, D. L. (1991). The innervation of lymphoid tissue. In R. Ader, N. Cohen & D. L. Felten (Eds.), *Psychoneuroimmunology* 2nd ed., (pp. 27–70). New York, NY: Academic Press.

Flaherty, D. K., Wagner, C. A., Gross, C. J., & Panyik, M. A. (1997). Aging and lymphocyte subsets in the spleen and peripheral blood.

Immunopharmacology and Immunotoxicology, *19*, 185–195.

Fricchoine, G. L., & Stefano, G. B. (1994). The stress response and autoimmunoregulation. *Advances in Neuroimmunology*, *4*, 13–27.

Harden, C. L., Daras, M., Tuchman, A. J., & Koppel, B. S. (1993). Low amplitude EEGs in demented AIDS patients. *Electroencephalography and Clinical Neurophysiology*, *87*, 54–56.

Hardt, J. V., & Kamiya, J. (1978). Anxiety change through electroencephalographic alpha feedback seen only in high anxiety subjects. *Science*, *201*, 79–81.

Johnson, L. C., Seales, D. M., Naitoh, P., Church, M. W., & Sinclair, M. (1979). The effects of flurazepam hydrochloride on brain electrical activity during sleep. *Electroencephalography and Clinical Neurophysiology*, *47*, 209–321.

Klosterhalfen, W., & Klosterhalfen, S. (1983). Pavlovian conditioning of immunosuppression modifies adjuvant arthritis in rats. *Behavioral Neuroscience*, *97*, 663–666.

Langewitz, W., Ruttimann, S., Laifer, G., Maurer, P., & Kiss, A. (1994). The integration of alternative treatment modalities in HIV infection—The patient's perspective. *Journal of Psychosomatic Research*, *38*, 687–693.

Lutgendorf, S. K., Antoni, M. H., Ironson, G., Klimas, N., Kumar, M., Starr, K., … Scheiderman, N. (1997). Cognitive-behavioral stress management decreases dysphoric mood and herpes simplex virus type 2 antibody titers in symptomatic HIV-seropositive gay men. *Journal of Consulting and Clinical Psychology*, *65*, 31–43.

Madden, R. E., & Kirsche, D. L. (1987). Low intensity intracranial electrostimulation improves human learning of a psychomotor task. *American Journal of Electromedicine*, pp. 41–44.

McCain, N. L., Zeller, J. M., Cella, D. F., Urbanski, P. A., & Novak, R. M. (1996). The influence of stress management training in HIV disease. *Journal of Nursing Research*, *45*, 246–253.

Miller, A. H. (2010). Depression and immunity: A role for T cells? *Brain, Behavior and Immunity*, *24*, 1–8.

Miller, V., Mocroft, A., Reiss, P., Kaglama, C., Papadopoulos, A. I., Katzenstein, T., … Lundgren, J. D. (1999). Relations among CD4 lymphocyte count nadir, antiretroviral therapy, and HIV-1 disease progression. *Annals of Internal Medicine*, *130*, 570–577.

Moldofsky, H. (1989). Sleep and fibrositis syndrome. *Rheumatic Disease Clinics of North America*, *15*, 91–103.

Peniston, E. G., & Kulkokosky, P. J. (1991). Alpha-theta brainwave neurofeedback therapy for Vietnam veteran with combat-related post-traumatic stress disorder. *Medical Psychotherapy*, *4*, 47–60.

Saxby, E., & Peniston, E. G. (1995). Alpha-theta brainwave neurofeedback training: An effective treatment for male and female alcoholics with depressive symptoms. *Journal of Clinical Psychology*, *51*, 685–693.

Scheibel, A., Conrad, T., Perdue, S., Tomiyasu, K., & Wechsler, A. (1991). A quantitative study of dendrite complexity in selected areas of the human cerebral cortex. *Brain and Cognition*, *12*, 85–101.

Schellenburg, R., Schwarz, A., Knorr, W., & Haute, C. (1992). EEG brain mapping. A method to optimize therapy in schizophrenics using absolute power and center frequency values. *Schizophrenia Research*, *8*, 21–29.

Schummer, G. (1996). Self-regulation of the immune system. Megabrain Report. *Journal of Mind Technology and Optimal Performance*, *3*, 30–39.

Smith, R. B., & Shiromoto, F. N. (1992). The use of cranial electrotherapy stimulation to block fear perception in phobic patients. *Journal of Current Therapeutic Research*, *51*, 249–253.

Solvason, H. B., Ghanta, V. K., & Hiramoto, R. N. (1988). Conditioned augmentation of NK cell activity: Independence from nociceptive effects and dependence on interferon-beta. *Journal of Immunology*, *140*, 661–665.

Sommershof, A., Aichinger, H., Engler, H., Adenaur, H., Catani, C., Boneberg, E., … Kolassa, I. (2009). Substantial reduction of naïve and regulatory T cells following traumatic stress. *Brain, Behavior, and Immunity*, *23*, 1117–1124.

Sterman, M. B. (1996). Physiological origins and functional correlates of EEG rhythmic activities. Implications for self-regulation. *Biofeedback and Self-Regulation*, *21*, 3–33.

Striade, M., McCormick, D. A., & Sejnowski, T. J. (1993). Thalamocortical oscillations in the sleeping and aroused brain. *Science*, *262*, 679–685.

Tozzo, C. A., Elfner, L. F., & May, J. G. (1988). EEG biofeedback and relaxation training in the control of epileptic seizures. *International Journal of Psychophysiology*, *6*, 185–194.

Turner, B. J., Markson, L., & Taroni, F. (1996). Estimation of survival after AIDS diagnosis. CD4+ T lymphocyte counts vs. clinical severity. *Journal of Clinical Epidemiology*, *49*, 59–65.

Watson, C. G., & Herder, J. (1980). Effectiveness of alpha biofeedback therapy: Negative results. *Journal of Clinical Psychology*, *36*, 508–512.

Wilson, L. F., & Childs, A. (1988). Cranial electrotherapy stimulation for attention-to-task deficit. *American Journal of Electromedicine*, *12*, 93–99.