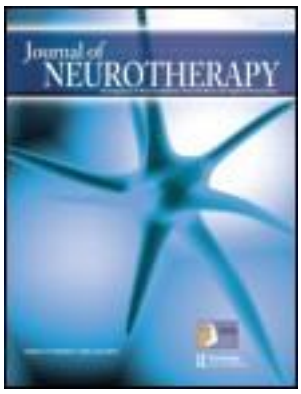

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Hemoencephalography-A New Therapy for Attention Deficit Hyperactivity Disorder (ADHD): Case Report

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Hemoencephalography– A New Therapy for Attention Deficit Hyperactivity Disorder (ADHD): Case Report

William Mize, MD

SUMMARY. *Background*. Hemoencephalography (HEG) is cortical circulatory biofeedback using refracted light tuned to oxygenated hemoglobin, emitted into the skull and detected at the scalp using a photoelectric cell. Red light at 660 nm is used as the probe, with changes in the returning refracted light representing changes in cortical circulation.

Method. A single-subject design case study was employed. TL, at age twelve, had a well-established diagnosis of ADHD given by pediatric neurologists, and required significant stimulant medication that was clinically effective. He was performing well in school on Concerta 36 mg at 7 a.m. and Ritalin 5 mg at 4 p.m. Off medication, he had significant abnormalities on IVA testing (Attention Quotient or AQ = 78) and in the quantitative electroencephalogram (QEEG). Using HEG, the patient engaged the system to exercise increases in signals corresponding to cortical circulation in the prefrontal cortex. QEEG, Continuous Performance Testing (CPT) and clinical status measurements were made

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before and after 10 sessions of HEG therapy. HEG exercise was typically given in weekly to bi-weekly sessions for 10 minutes in each of three standard prefrontal EEG locations: FP_1, FP_2 and FPz.

Results. During the 10 therapy sessions TL's HEG data showed positive gain indicating success at raising the biofeedback signal. Following the 10 sessions, TL showed a normal QEEG with improved Z scores for relative power and normal IVA testing *off* medication (mean AQ 99.75 ± 7.85 on three dates), which persisted in the 18-month follow-up. His medication was lowered to Focalin 2.5 mg twice daily.

Conclusion. This work documents a patient who showed clinically significant improvement after only 10 sessions using a new form of neurobiofeedback, hemoencephalography. If confirmed in controlled studies, this represents a breakthrough in treatment options for ADHD. Future studies should explore synergies between HEG and EEG neurofeedback therapies.

KEYWORDS. Hemoencephalography, neurotherapy, neurofeedback, ADHD, prefrontal cortex, cortical circulatory biofeedback, biofeedback

INTRODUCTION

Attention Deficit Hyperactivity Disorder (ADHD) Physiology and Treatment Options

Attention Deficit Hyperactivity Disorder (ADHD), along with its silent partner Attention Deficit Disorder (ADD) and the many accompanying co-morbid conditions (oppositional behavior, learning disabilities, depression, anxiety, bipolar disorder, tics, etc.) and masquerading conditions (auditory processing problems, attachment disorder, depression/anxiety alone, toxic encephalopathies, dietary sensitivities, nutritional deficiencies, mental retardation and others) affects about five percent of the population worldwide (McGough & McCracken, 2000; Riccio & Reynolds, 2001). The condition is so heterogeneous that it cannot be characterized simply using neuroanatomic, clinical, genetic or physiological criteria alone (Biederman & Faraone, 2002; McGough & McCracken, 2000; Schweitzer et al., 2000). For diagnosis, clinicians typically rely on questionnaires listing symptoms and the DSM IV criteria, which are behav-

ioral and subject to interpretative bias. Functional magnetic resonance imaging work shows that multiple brain loci are involved in the mediation of attention problems (Ernst et al., 1999; Posner & Raichle, 1998; Zametkin et al., 1990) and pharmacological studies show that no one model of brain chemistry accounts for all of the cases or range of symptoms (Vaidya et al., 1998). Indeed, there is lack of agreement among theorists concerning exactly what "attention deficit" means (Barkley, Grodzinsky, & DuPaul, 1998; Mirsky, 1987; Williams & Boll, 1997; Lee, 1991). Thus, any one treatment method cannot be expected to serve all whether it is pharmacological, electrophysiological, or behavioral. Similarly, measuring the outcome of treatment is difficult and for the most part consists of behavioral inventories and subjective reports of better behavior and higher grades. Some clinicians monitor progress with computer-based continuous performance tests (discussed below) or other neuropsychological testing and some use the QEEG (Monastra, Monastra & George, 1999), or SPECT scans (Sieg, Gaffnew, Preston, & Hellings, 1995). But these methods do not have clear clinical correlations *tightly* tied to their datum (McGough & McCracken, 2000). The clinician is generally left with behavioral inventories and subjective histories as the principal method of marking improvement.

While clinicians agree that a multi-modal approach is both necessary and beneficial given the individual needs of clients, the recently celebrated Multimodality Treatment of ADHD (MTA) collaborative study showed that comprehensive treatment including medication, behavioral advice and counseling was not measurably better than medication alone for ADHD simplex (Swanson, Lerner, March, & Gresham, 1999). From a practical viewpoint, almost all children with ADHD receive medication, which remains the single most consistently effective treatment available. This is distressing to those in our society who want to move away from a chemical culture and whose children do not tolerate the medications or receive only marginal benefits. Parents desiring non-medical treatments do not have cost-effective, proven alternatives. Many seek dietary interventions, which have been proven helpful in only about one percent of cases (Baumgaertel, 1999). It is beyond the scope of this paper to discuss alternative treatment modalities as a whole. However, many take hope in neurobiofeedback in one or another of its many incarnations: SMR, Theta/Beta, Alpha, and others (Shouse & Lubar, 1978, 1979; Lubar, 1991; Monastra, Monastra, & George, 2002; Lubar, Swartwood, Swartwood, & O'Donnell, 1995; Alhambra, Fowler, & Alhambra, 1995; Rossiter & La Vaque, 1995). Despite encouraging results and clear clinical benefits in many cases, the greater public and the

medical community in particular remain skeptical (Ramirez, Desantis, & Opler, 2001; Arnold, 2001). In part, this is a pragmatic concern based on the perceived cost of therapy, the number of sessions required (twenty to eighty) and the relative dearth of well-controlled, well-designed studies demonstrating efficacy. Thus, EEG biofeedback has remained at the fringe of the treatment world for ADHD. Despite these problems, neurotherapy remains an important primary and adjunctive treatment for ADHD and other disorders precisely because it promises an alternative to medication.

The newest of these technologies, Hemoencephalography (HEG), appears to be especially promising because of its relatively short timeline for efficacy. Toomim et al. (2004) found that clients as a group improved TOVA™ impulsivity scores 12% following 10 sessions of HEG therapy. I am pleased to report similar gains in this paper, demonstrated for the attention domain measured by the IVA in a single client serving as his own control. HEG purports to improve cortical circulation directly, in contrast to EEG biofeedback, which modulates the epiphenomenon of wave patterns and thus can only indirectly influence functional circulation. Since ADHD is known to be associated with cortical circulatory and metabolic deficits in the prefrontal areas, it is reasonable to assume that any therapy increasing cortical circulation in those areas may improve clinical functioning. While they are just beginning to be documented, the prefrontal area may impact many brain functions in addition to attention. QEEG data supplement IVA testing and may indicate broader, though for now nonspecific, improvements. Like the other forms of neurotherapy, HEG needs controlled validation. This case report is a step in that direction.

Ways of Evaluating ADHD

Behavioral questionnaires such as the ADHD-IV, BASC, CBCL, Conners, and The Diagnostic Rating Scale (McGough & McCracken, 2000) provide the core tools to clinicians regarding quantifying symptoms, with the Conners family of forms being the most popular. Such forms, while helpful, are also problematic because different observers focus on subsets of behaviors of special concern to them or on circumscribed time frames of which they may be particularly aware. The expectations and tolerance of observers to behavioral variation is wide, introducing a host of biases to their scores.

In contrast, continuous performance tests (CPTs) are very objective procedurally, but not thought to be ecologically valid, being merely a

proxy for classroom behaviors and other clinical concerns. CPTs of various kinds have been used by investigators for almost 50 years (Rosvold, Mirsky, & Sarason, 1956) and by clinicians more heavily in the last ten years to quantify and track the symptoms of ADHD patients (Riccio & Reynolds, 2001). There are a plethora of different CPT systems, which measure different cognitive functions related to the elusive attention function clinicians hope to improve and for which none can claim to be the gold standard. The most common and best validated methods are the Conners™ (Conners, 1995; Barkley et al., 1992), the IVA™ (Edwards, 1998), the Gordon system™ (Gordon, 1983; Saykin et al., 1995; Gordon & Barkley, 1998), and the TOVA™ (Greenberg, 1993), all of which refer to normative data in scoring. While these CPTs offer the promise of quantitative results and do give a "number," they are dependent on state of arousal, effort, quality of sleep the prior night, and other factors such as environmental distractions, medication timing, and exposure to nicotine and caffeine, any of which may contribute to variance in performance. Thus, the clinician must interpret results carefully and understand that episodic variation may have no meaning at all when the clinician is attempting to evaluate treatment efficacy. Many clinicians have experienced cases where a child does poorly on the CPT but is doing well clinically, and contrastingly, the child who does well on the CPT, but has clear clinical impairments. Indeed, false positives and false negative assessments have been formally described when CPTs are used in isolation (Trommer, Hoeppner, Lorber, & Armstrong, 1988). Nonetheless, *most* children who do poorly in "life/school" do poorly on CPTs and children doing well clinically do well on CPTs. In my experience, they are a helpful adjunct for monitoring clinical progress.

In my practice, I use the IVA CPT, which presents both auditory and visual target stimuli interspersed. While the test doesn't put a number on this factor, it clearly tests the ability of the client to shift modes and to interpret auditory information interspersed with visual information; whereas, unimodal sensory tests do not. There are advantages and shortcomings to either approach. I feel that the mixed modes in the IVA are a better proxy for the classroom than the unimodal tests.

Brain imaging using functional MRIs and SPECT scans or other technologies offer great promise for precision of clinical status, but are not practical tools for monitoring progress because of their cost, invasiveness and inconvenience. Until better and cheaper imaging technologies are available, the QEEG and related imaging systems offer alternatives. The QEEG has the same range of day-to-day context problems enumer-

ated for the CPTs above and additionally is subject to technical problems which can degrade the signals, such as poor electrode placement, faulty equipment, temporary changes in the electromagnetic environment, circadian variation and more. Like the CPTs, QEEGs are a helpful tool despite their limitations.

Overview of HEG

The HEG signal is the ratio of a red and infrared light signal transduced by a photoelectric amplifier. The red light signal is tuned to chromophores in oxygenated hemoglobin and taken as a measure of blood flow. The second, an infrared wavelength, is used as a reference, being fairly constant and independent of blood flow. The physics of this system has been studied intensively (Jobsis, 1977; Obrig, 2003; Soul & DuPlessis, 1999; Villringer & Chance, 1997). The apparatus used in this case has been designed to capture information reflecting cortical blood flow in an area of approximately 1 cm^3. The device alternately emits light signals into the skull below the placed headband (one red and one infrared) and then detects light, which is partially absorbed and then refracted back to the surface of the scalp. This signal forms the basis of the biofeedback graphic, which the subject voluntarily increases during a therapy session.

The cortical blood flow reflected in the averaged HEG signal is sampled at a rate of at least 16 times per second depending on the system, and is in the form of a variable line graph. An increase in the signal is taken to represent an increase in cortical circulation at that location. The cortical circulation naturally fluctuates about 10% from moment to moment throughout the day, depending on activity context and arousal. H. Toomim reports background gains of about 10% (personal communication, July 17, 2003) based on the absolute minimum within a 10-minute segment, which is an alternative to using the first 10 seconds of a segment as the minimum. Using the *absolute* minimum as the "initial value" in this study rather than the *actual* initial 10-second segment means would have generated much higher "gains" than reported here. I have used the initial 10-second segment baseline values because I believe it to be a more appropriate and conventional basis for defining gain from baseline in the context of active therapy than an absolute minimum elsewhere in the data stream. Increases beyond the baseline, whether stimulated by functional exercises, HEG, or other means, are thought to encourage tissue development. Most subjects are able to produce regu-

lar brief increases in the signal with a minimum of training. Toomim et al. (2004) in a study of 28 clients reported routine session gains of about 10% in a given 10-minute segment (based on the initial segment definition of gain), indicating general success in consistently improving the HEG signal strength during a therapy session. The performance of a client during training sessions typically waxes and wanes, but most sustain a positive change for the majority of time in a session.

Case Study

TL presented initially to me on February 1, 2000 in the seventh grade at chronological age (CA) 12 years and 3 months. He had a standing diagnosis of ADHD first given by a child neurologist in April of 1998 at CA 10 years and 6 months. The child neurologist had followed him since November 21, 1996. TL had a history of fidgety behavior requiring close supervision in his early elementary school years and grades that deteriorated from As and Bs through the fourth grade to Cs and some Ds and Fs (not reflected by yearly average) in the fifth grade. TL's fifth grade work was especially poor for homework compliance. He had strengths in math and science and weaknesses in reading comprehension. He improved on Ritalin 10 mg twice daily (BID) and made mostly Bs and Cs in the sixth grade, but was felt "not to be working up to his potential." He later consulted another child neurologist in July of 1999 at CA 11 years, 9 months, who titrated his Ritalin to 20 mg slow release and noted concurrent problems with headache and depression.

On initial consultation with me, TL had symptoms of ADHD and mild symptoms of depression, not felt to be clinically significant. Verbal weakness, but not learning disability (LD) was confirmed on the WISC-III and WIAT on August 3, 2000 (CA: 12 years, 10 months).

WISC Results:	Verbal Quotient (VQ)	119
	Performance Quotient (PQ)	126
	Full Scale IQ	124

WIAT achievement testing yielded the following standard scores:

Reading composite:	110	Written expression:	86
Math composite:	118	Writing composite:	85
Spelling:	89		

TABLE 1. Pre-HEG IVA Testing

	AQ*	Aud.	Vis.	**RQ***	Aud.	Vis.	
10-11-2000	96	96	98	132	124	133	Ritalin 20SR in a.m., test 2 p.m.
11-07-2000	**78**	**81**	**79**	**121**	**132**	**107**	**Off meds test 10 a.m.**
01-17-2001	95	99	92	119	125	111	on Concerta 18 test 1:30 p.m.
02-08-2001	90	97	85	124	124	119	on Concerta 36 test 1:30 p.m.
On-medication Means	93.66	97.33	91.66	125	124.33	121	
On-medication St. Deviation	2.62	1.24	5.31	5.35	0.47	9.09	

Weak attention scores off meds and postiive effects of medication are observed.

Follow-up cognitive testing on November 16, 2002 using the Wide Range Intelligence Test (WRIT) was more suggestive of verbal LD and yielded scores of:

WRIT: VQ 104 PQ 127 IQ 118

TL was clearly above average in his general cognitive abilities with weaknesses in the verbal domain. IVA testing (continuous performance testing) was used to quantify TL's attention deficits. Initial IVA testing on October 11, 2000 is seen in Table 1.

* RQ response control quotient (impulsivity) reported as a global score with auditory and visual components.

* AQ: global attention quotient, also with auditory and visual components.

This indicated good medication efficacy on an instrumental test. However, due to afternoon challenges at school, TL was then given an additional 10 mg of Ritalin at noon. These CPT results show that TL had *clinically significant attention deficits off medication and normal testing on medication.* His impulsivity scores were above average in both conditions. On March 6, 2002 TL was put on Concerta 36 mg plus Ritalin 5 mg at 3 p.m. and by April 16, 2002 he was on the honor roll.

Hypothesis

Brain function and attention testing improves following a course of HEG cortical biofeedback applied to the prefrontal area.

METHODS

Equipment

The HEG system used in this study is standard equipment from the Biocomp Research Institute and included a flexible headband consisting of a photoelectric sensor and two photo-emitting diodes connected to a signal processing amplifier station designed to interface with Procomp™ and other bio-hardware systems. The light emitting diodes were tuned to wavelengths of 660 nm and 850 nm. The HEG hardware was linked to Thought Technology's Biograph Procomp Plus encoder and to a Dell™ laptop using Biograph™ software that provided the biofeedback interface with the patient. The visual interface was a simple line graphic. The Biocomp™ system sampled data at 32 times per second. Data files generated and saved by the Biograph™ software were exported to Microsoft Excel™ for analysis. The QEEG was done on a Lexicor™ machine and analyzed with the Thatcher Lifespan database. The QEEGs were recorded and interpreted by Joseph N. O'Donnell, PhD. Further QEEG analysis was provided by Robert Thatcher, PhD, using the Neurostat™ program.

The IVA CPT results are summarized for the domains of impulsivity (response control quotient; RQ) and inattention (attention quotient; AQ) and results for each of those domains are further broken down into auditory and visual components. Target stimuli are presented in both low frequency and high frequency formats (the numeral "1" vs. the numeral "2") with visual and auditory presentations intermixed in pseudorandom order. The IVA is normed at 100 as the average performance of a normal person of a given age and gender.

HEG Data Definitions in This Study

Absolute HEG readings have such high session-to-session variance that the readings alone have limited meaning. However, to give a somewhat objective measure of what takes place during a therapy session, the mean amplitude of HEG signals for a given position can be recorded

and analyzed, as well as mean "gains" per session. Gain here is defined as:

$$\text{Gain} = [(\text{segment average})/(\text{initial average})] - 1$$

"Segment average" is the overall total segment mean HEG value and the "initial average" is the mean of an initial segment of arbitrarily chosen length, generally 8 to 10 seconds. When the equipment is turned on and the headband put in place, the system takes some time (typically less than 30 seconds) to "settle down" to what will be a realistic reading for a given position. If the headband requires positional readjustment (due to client discomfort, headband tension, etc.) there must be further delays before data recording and therapy can begin. As with EEG artifacting, the clinician must interpret precisely when to begin data recording (what part of the initial data may be considered valid) and when to end it. Because each skull/brain position receiving HEG signals is distinct in its physiology, data analyses must be separate for each.

Since a therapy session consisted of applying the HEG technique to three prefrontal locations (Fp_1, Fp_2 and FP_z), the HEG data as a whole had to be divided into three major segments. In these analyses, the initial segment value was chosen by the investigator to be of 10 seconds duration and generally began with the first clear minimum recorded in the first 30 seconds after putting the headband in place and starting the system. Preliminary calculations show that using an 8-second bound for the definition of the "initial" segment gave similar but higher gain calculations. The 10-second measure was chosen because it was felt to be more conventionally universal than the 8-second definition and appeared more likely to allow comparisons with data gathered in future studies in this field. Since the mean HEG values for each position typically vary somewhat, it was easy to identify transitions between the segments. Because the system was "paused" between segments, brief wide fluctuations in the signals served as clear markers of a change in headband position. Gain data derived from both 8- and 10-second segments are available on request. Data recording for analysis was terminated for the segment as a whole when the data indicated a clear disruption at the end of the segment, such as when the headband was removed and wide "unrealistic" fluctuations in values resulted. All intervening data was included in the analysis in this case study, regardless of internal fluctuations. Thus, the investigator identified a "clean" starting point and "clean" ending point for the data and accepted all intervening values. This was done for simplicity of analysis, though it is clearly imperfect.

Each therapy session thus provided three segments from which to record and analyze HEG data.

Therapy Procedure

The subject and his mother were brought into a florescent-lit (not dark) clinic examining room where the equipment was behind closed doors, but subject to low level background noise from the rest of the clinic. There were no pre-therapy "relaxation" measures or other preparations engaged, and no control or measure was taken for the state of arousal of the patient, which was generally quiet and alert. The therapist acted as a coach in the initial sessions and adjusted the position of the headband after each 10-minute therapy segment so that the target areas $FP_{1,}$ then $FP_{2,}$ then FP_z each received treatment. Note that this is a different order than the one used by Hershel Toomim in his original study (i.e., $FP_{1,}$ then $FP_{z,}$ then FP_2). I chose this order hoping to maximize the "sympathetic" effect reported by Toomim et al. (2004), where symmetric positions in the contra-lateral hemispheres, such as FP_1 and FP_2, were noted to passively increase when HEG was applied to one of them. The client was reminded to breathe normally and to use his "thinking" and "desire/will" to increase the signal. The signal was a simple line display with HEG magnitude on the ordinate and time on the abscissa. The system produced a tone each time the signal rose above the previous level by a small increment. Verbal reinforcement was given when minor successes occurred, usually by a simple "good" or "more of that." TL demonstrated the ability to sustain an increased HEG signal from the first session. Once the subject understood the task, he was left alone to work on increasing his HEG signals without the help of the therapist. The therapist was typically present about 20% of the therapy time though a parent was generally, but not always, present and sometimes offered verbal encouragement. When the 10-minute segment was complete, the system was paused, with the client given less than 5 minutes to rest and the headband readjusted to the new position.

RESULTS

HEG Session Summary

On June 12, 2002, neurotherapy sessions were initiated using Hemoencephalography (HEG). TL was given 10 sessions of HEG consisting

of three 10-minute segments in each of three prefrontal cortex locations (FP_1, FP_2, and FP_z), in that order. The therapy was given from June 12, 2002 through October 17, 2002, a period of about four months. Therapy was delivered at the following intervals in days: 35, 21, 8, 7, 7, 6, 12, 22, and 7, with an average interval of 13.8 days. The initial interval was longer to allow the family time to accomplish the initial QEEG appointment. An initial QEEG was performed by Joseph O'Donnell, PhD, on June 21, 2002 and found to have the following mild abnormalities, confirming CNS dysfunction. His clinical impressions were:

"The various analyses highlight significant CNS dysfunction: Decreased asymmetry: L < R, beta band; Coherence irregularity: (central beta); Phase irregularities: (all frequencies)."

The average minutes of HEG neurotherapy per session per site were:

FP_1: 11.8 minutes FP_2: 9.8 minutes FP_z: 10.1 minutes.

Total session means for the HEG ratio signal were:

FP_1: 89.53 ± 20.6 FP_2: 81.24 ± 19.25 FP_z: 67.40 ± 9.00

Mean session gains [(session average/first ten second average)−1]:

FP_1: .106 ± .050 FP_2: .070 ± .057 FP_z: .021 ± .037

TL had positive gain for most segments, with the exception of FP_z, which had negative gain for the first, second, third and ninth sessions. If those sessions are omitted from the analysis, the average gain for FP_z rose to .043 ± .032. These data also suggest a fatigue effect on gain across a given therapy session, which was worse in the initial sessions (data available from author on request). The improvement in gain at FP_z suggests TL became more effective in raising HEG signals with experience, or that he learned to overcome fatigue. The order of HEG therapy was always FP_1, then FP_2, and then FP_z. TL was tested off medication following the completion of HEG therapy (October 17, 2002) on four dates (see Table 2). Because TL inadvertently took Focalin the morning of testing on November 13, 2002 (AQ = 115), he was re-tested off medication on November 16, 2002 (AQ = 109). Off-medication attention measures as reflected by the IVA show normal scores on all of four of the medication free dates (mean AQ = 99.75). These results suggest

TABLE 2. Post-HEG IVA testing

	AQ*	Aud.	Vis.	**RQ***	Aud.	Vis.	
11-07-2000	**78**	**81**	**79**	**121**	**132**	**107**	**PRE HEG; Off meds; test 10 a.m.**
11-13-2002	115	113	115	86	82	93	7:30 a.m. Focalin, test: 1:30 p.m.
11-16-2002	**109**	**104**	**112**	**99**	**105**	**94**	**Off all meds test 10:30 a.m.**
4-16-2003	106	108	103	97	111	83	Off meds
10-23-2003	93	98	90	106	114	97	Off meds 10 a.m.
4-14-2004	91	94	89	106	102	110	Off meds test 9:15 a.m.
Off-Med Post HEG Means	99.75	101	98.5	102	108	96	
Off-Med St. Deviation	7.85	5.38	9.55	4.06	4.74	9.61	

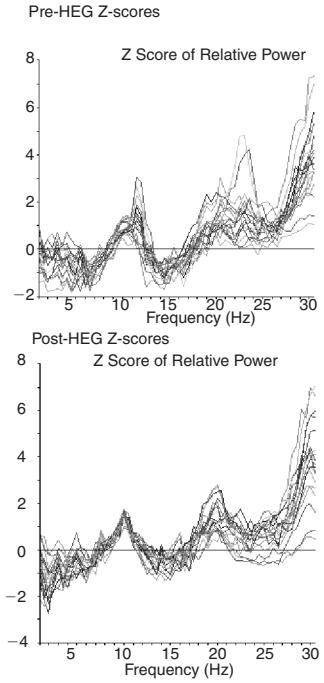
Improvement in attention scores off medication is noted.

marked improvement in attention scores off medication following HEG therapy.

A follow-up QEEG off medication was performed by Dr. O'Donnell on December 22, 2002 and was substantially normal: "The QEEG is overall normal with some borderline results that may not be of clinical significance." An examination of Z scores for relative power pre- and post-HEG shows a general flattening of the curves indicating QEEG changes towards normal (see Figure 1). Each of the colored lines in the figure represents a different site on the scalp in the 10-20 scheme for QEEG. The tracings are so interwoven that individual sites are difficult to discern. Generally the absolute power of the post-HEG QEEG was greater and there were fewer significant Z scores in relative power analysis generated from the NeuroGuide™ software (see Figure 1). One can see that there are fewer aberrant tracings representing relative power in the post HEG figure and that the tracings are more tightly interwoven and closer to Z = 0. Of the various changes in relative power, the most generally consistent was increased alpha.

IVA testing at the six-, twelve- and eighteen-month follow-up (April 16 and October 23, 2003 and April 14, 2004) confirmed the positive results following HEG therapy. Despite these positive laboratory results and subjective reports from TL's mother, who felt that his general ability to manage schoolwork and homework was better, TL felt some residual clinical challenges in school and at home and requested that he remain on a low dose of Focalin. His grades on Concerta 36 mg were Bs and Cs before HEG. While he may have passed academically off medication, our therapeutic goal was *optimum* function on the least medica-

FIGURE 1. Pre- and post-HEG relative power Z-scores



tion necessary, not minimally acceptable function *off* medication. TL continues to do as well in school with a B to C grade average on Focalin 2.5 mg BID. This represents a substantial reduction in the dose of his stimulant medication.

DISCUSSION

TL's improvement is based on equivalent school performance on minimal medication, where historically he had significant ADHD, which required substantial doses of stimulant. Indeed, correction of inadequate dosing at the time of initial consultation appears to be a major reason for his academic improvement prior to HEG therapy. TL's IVA performance *on medication* prior to HEG therapy was stable with an RQ mean of 125 ± 5.35 and an AQ mean of 93.66 ± 2.62 (see Table 1). There were no trends in his testing results to suggest either systematic improvement with practice, nor deterioration due to malingering or dis-

content. Similarly, after HEG, his performance off medication (excluding the afternoon test following the morning dose of Focalin) was also stable with a mean RQ of 102 ± 4.06 and a mean AQ of 99.75 ± 7.85. All post-HEG IVA domain data was normal except for the visual RQ domain on April 16, 2003 of 83. That data point fell just below the 85 point cutoff for clinical abnormality, but was within 1.5 standard deviations of the mean for the RQ visual domain off medication (91.33 ± 6.01) and as one data point in eighteen, appears to be aberrant. The IVA is estimated to have a standard error of less than 10% on test/retest studies whereas the magnitude of change in the *attention* domain reported in this paper is about 20% and at least three standard deviations in magnitude. TL's improvement is supported by normal IVA testing off medication for 12 months, and normalization of his QEEG (same equipment, same clinician, and same database).

It would appear that HEG is responsible for this improvement. However, future studies must be designed to eliminate possible confounding factors present in this case. Generally, the patient's baseline measures should be taken immediately proximal to the onset of HEG therapy. This would eliminate considerations due to brain maturation, possible changes in the use of executive functions such as improved study skills, and other environmental influences or stressors. Care must be given to assess more explicitly the mental status of the patient regarding possible opposition, poor effort, malingering and depression, none of which were thought to be present in this case.

Of potential concern is the deterioration of impulsivity ratings that accompanied the improvement in attention ratings on the IVA. TL's RQ scores fell from a superior rating to average. If this change is real, it suggests more impulsivity; however, all the scores are completely average in performance, suggesting that those changes lack clinical significance. No one would seek therapy of any kind with average impulsivity ratings. The author wonders if the superior early performance on impulsivity measures reflected an abnormal hypervigilance of some kind that normalized following HEG therapy.

A look at the trend of IVA values following HEG therapy suggests a gradual rising of RQ and falling of AQ towards the pre-therapy values as if TL's brain is slowly returning to its former state. This trend appeared to level off at the 18-month follow-up evaluation, suggesting stable improvement following HEG therapy.

Assuming HEG is indeed responsible for TL's progress, one can look for procedural factors that could modulate possible outcomes. Is the

timing of therapy an issue? Is FP_2 more important than FP_1 for therapy? It is noted that TL's HEG levels at FP_z were considerably less than the expected population mean of 100 ± 20. Should therapy have spent more time at FP_z? His measures at FP_2 were lower than at FP_1 consistent with imaging reports of metabolic deficits at FP_2 in ADHD patients. If the HEG effect is mediated by circulatory improvements, one might expect HEG values to rise not only in a given session, but also across sessions, implying improvements in baseline circulatory function. Or is the clinical effect mediated by both neural *and* circulatory changes? Contrary to expectation, during the course of HEG, there was no pattern or trend in the mean absolute HEG values in the ten sessions.

Would the data have been more regular if therapy sessions took place in a darkened room? Could short term improvements in baseline cortical circulation be too small to detect using HEG measurements with the current technology? The variance in HEG signals from session to session suggests this may be the case, but further studies using SPECT imagery might be helpful here. There were position-to-position and day-to-day differences that make absolute measurements impossible to interpret meaningfully with the current modeling of the system. Finally, theoretical concerns have been raised concerning the degree of hemoglobin concentration in an individual (Kurth & Uher, 1997), further contributing to variability in meaning for the signals. While such issues create problems for the interpretation of absolute measures, they have no practical bearing on in-session *gains*, which are relative measurements with relatively modest session-to-session ranges of activity.

In this case study HEG "gain" was not equal for the three therapeutic sites. FP_1 was greater than FP_2 than FP_z ($.106 \pm .050 > .070 \pm .057 > .021 \pm .037$), though the standard error of measurement was generally larger than these differences. A series of patients will be needed to verify this trend. If true, the decreasing gains suggest that there is a "within session" physiological fatigue effect for gain in each subsequent 10-minute segment of therapy. Patients sometimes report physical fatigue following HEG therapy. Toomim (personal communication, October 31, 2001) reports that if HEG levels drop significantly due to physical fatigue, a 20-second rest period usually restores performance, and that if this persists, he advises the therapy segments are shortened to 5 to 7 minutes. Further, it is conceivable that those associated physiologically mediated "sympathetic" rises in FP_2 and FP_z on a given day immediately following prior therapy at FP_1 could raise the starting values at FP_2 and FP_z and thus decrease the *gain* at FP_2 and FP_z during therapy *at*

those positions. Subsequent experiences in my clinic measuring baseline HEG values in multiple positions before starting therapy with other patients suggest that this phenomenon is quite common and regularly results in *baseline rises* for the positions following therapy at FP_1. Future studies might anticipate this problem and measure HEG baseline levels in all three positions prior to beginning therapy for any position in the session. This may necessitate even more careful placement of the optodes since pre-therapy baseline measurement locations are disrupted when therapy is delivered at FP_1, necessitating repeat positioning for FP_2 and FP_z when therapy is actually delivered at those locations.

The mean interval between sessions in this case was 13.8 days, while the median interval was 8 days and the mode was 7 days. It remains unknown what therapy schedule might yield optimal results. Preliminary data from the Toomim et al. (2004) study shows that sessions less than 4 days apart in a series of 10 sessions are less effective in the short run than sessions at longer intervals. This suggests that the session's influence on the brain extends during quiescent times or that periods of rest are important, possibly for growth in neural connections to occur. If one assumes that HEG stimulates neural growth as has been suggested by Toomim et al. (2004), then time is needed for these connections to develop and mature.

It is unknown whether the key therapeutic event is actually accomplishing an increase in the HEG signal or whether it is something less tangible, like the effort involved for which the signal is just a proxy. Special studies, possibly involving sham or artificially amplified HEG signals would be needed to address that difficult issue. However, if one assumes that growth in neural connectivity secondary to HEG therapy yields the beneficial effect, then again, absolute HEG levels are of secondary importance relative to within session gains and the resulting neural growth that follows.

Generally, one would postulate a relationship between gain and time to outcome or gain and time *in a given position* to outcome, but this would require a population study rather than a case study or a special "double optode" headband allowing passive measurements at the sympathetic site. Establishing a relationship between particular position gains and outcome would strengthen the theoretical basis for HEG therapy. Practitioners contemplating case studies in HEG should consider strategies that use baseline measures in multiple sites prior to each therapy session, and give great care to precision in optode placement. The skull varies in thickness from front to side and top to bottom, and con-

sideration should also be given to whether the emitters are consistently medial or lateral relative to the sensor and placed without "tilt." If skull thickness has any bearing at all then randomizing the placement of the signal source or varying the "tilt" rather than optimizing optode placement with consistent positioning of the emitter would diminish the power of positional data for gain by increasing the variance of the recorded signals due to positional errors. Obtaining good results without these considerations implies a more robust treatment effect, but might impede valuable, but more subtle conclusions based on positional differences.

The intervention described in this study may be interpreted as conservative, though pragmatic, due to the low intensity of therapist involvement. Since both HEG and EEG neurotherapy have demonstrated efficacy, it is tantalizing to consider the possible benefits of combining these therapies. Might HEG in tandem with EEG neurotherapy augment its efficacy or time efficiency? Similarly, HEG might amplify gains intrinsic to other kinds of cognitive interventions. Future studies must determine the relative power and effect permanence of the two modalities in a wider spectrum of clinical problems and give further definition to the place of each in the armamentarium of the neurotherapist.

CONCLUSION

Ten sessions of HEG applied in 10-minute segments to FP_1, FP_2 and $FP_{z,}$ in that order, appear to have produced significant changes in attention as measured by the IVA (normal functioning off medication with the mean AQ of 99.75). These results are supported by normalization of the QEEG and continued positive clinical reports of normal behavioral symptoms and academic progress on minimal stimulant medication. Stimulant medication was reduced from starting levels of Concerta 36 mg at 7 a.m. and Ritalin 5 mg at 3 p.m. to Focalin 2.5 mg BID. The efficiency of HEG in number of sessions compared to other forms of neurotherapy such as EEG biofeedback, suggests that it may become the first realistic and pragmatic alternative to medication treatment alone. Combining the modalities may prove to be even more powerful. Controlled studies are needed to validate the promising findings in this emerging technology.

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