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Place of electroencephalograpic biofeedback for attention-deficit/hyperactivity disorder

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Place of electroencephalograpic biofeedback for attention-deficit/hyperactivity disorder

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Although methodological weaknesses limited early research into electroencephalograpic (EEG) biofeedback (EBF) for treatment of attention-deficit/hyperactivity disorder (ADHD), recent stronger randomized controlled trials have provided substantial, but not yet conclusive, empirical support. Additional support is found in research on functional magnetic resonance imaging (fMRI) feedback and brain—computer interface (BCI) models, which involve feedback-guided learning to achieve control over neural activation. Given the established clinical reality that a large percentage of patients with ADHD

either do not receive or do not sustain medical treatment, EBF is best viewed as an evidence-based treatment that is typically employed in practice when medical treatment fails or is not accepted by the patient. Viewed in this light, EBF is making an important

clinical contribution in providing research-supported treatment to those who would otherwise remain untreated.

Few neuroscientists now doubt that we are able to exercise volitional control over neural functioning when given real-time feedback. This phenomenon has been well established in two areas of recent neuroscience that together have been grouped under the name of real-time neuroimaging: BCI research and real-time fMRI (rtfMRI) feedback. While this research has generated considerable scientific and popular interest and excitement, it is

less often remarked or noticed that it validates the fundamental premise of EBF, also known as neurofeedback.

In the field of BCI research, this is most evident in studies using signals recorded at the scalp. A considerable training period is required to enable the patient to learn self-control over the selected parameter of the EEG signal [1–3]. Even with the use of sophisticated mathematical algorithms developed through systematic research to translate the neural signals captured by implanted electrodes into computer cursor movements [4], an initial

period of feedback-based learning was required for the human subject to gain control of the cursor [SERRUYA MD, PERS. COMM., 2006]. This feedback-guided learning is EBF training, pure and simple.

strategy...' Several studies of fMRI feedback have shown that participants were able to learn enhanced voluntary control over task-specific cortical activation when provided with feedback derived from rtfMRI. This form of feedback-guided learning has been demonstrated in several cortical areas [5–7].

Follow-up research on both BCI and fMRI feedback is now underway in numerous university centers and the field of real-time neuroimaging is an accepted subspeciality in neuroscience. However, despite the consensus on the viability of feedback-guided learning for cortical control, considerable controversy

continues to surround EBF as a clinical application of this strategy to alter patterns of cortical activation known to be deviant in ADHD.

There is, however, a growing and substantial body of evidence supporting the efficacy and clinical utility of this tool for treating the primary ADHD symptoms. Owing to significant methodological weaknesses in many of the early studies, the generalizability of their findings is limited. However, the more recent studies have successfully addressed many of these concerns.

Overall, more than 20 studies have been conducted involving over 700 subjects. Nine have been controlled trials, involving over 400 subjects, with comparisons to sham treatment, nontreatment and stimulant medication controls; these include five randomized controlled trials.

Two of these later randomized controlled trials utilized a double-blind sham-treatment control. In one study, 42 subjects were randomly assigned to experimental and sham-treatment control groups, with the groups well matched by demographic, diagnostic, intelligence quotient and achievement score variables. It employed well established and validated parent and teacher report measures of ADHD symptoms, a continuous performance test (CPT) and quantitative EEG (qEEG) and showed highly significant improvements on all three behavioral measures and the qEEG for the experimental but not the control group [8].

A second double-blind sham treatment study '...EBF is best viewed as an involved 31 subjects randomly assigned to EBF treatment, sham-treatment control and wait-list control [9]. Significant improvements were observed in the EBF treatment group, but not in that has substantial but not the sham or wait-list controls, with the latter two yet conclusive evidence of groups indistinguishable.

efficacy...' In another well-designed recent study, 20 ADHD subjects were randomly assigned either to an EBF experimental group (15 subjects) or a non-EBF control group [10]. Before and after the EBF training was completed, all subjects were given an fMRI scan while performing a Counting Stroop task, as well as cognitive and behavioral testing using the Weschler Intelligence Scale for Children-Revised digit span test, a CPT and the Conners Parent Rating Scale-Revised (CPRS-R). Converging evidence positron-emission tomography (PET) and fMRI studies has shown that the dorsal division of the anterior cingulate cortex (ACC) plays a pivotal role in the cognitive processes involved in the Stroop task; previous research has also demonstrated dysfunction in this area in subjects with ADHD while performing the Counting Stroop task [11].

After 40-h long EBF training sessions, both groups were rescanned under the same Stroop task and cognitive and behavioral measures were repeated. The EBF group showed significant increases in activation in the dorsal ACC, whereas the control group did not. The experimental but not the control group also showed significantly improved cognitive performance on the Stroop task, as well as significant improvements on the digit span, CPT and CPRS-R.

Overall, in this body of research, statistically significant improvements for experimental but not control groups have been documented using well-established measures. Effect size is similar to that shown with stimulant medication. Improvements in attention and impulsivity have also been documented in nonclinical subjects. Predicted parallel improvement in neurophysiological measures has been demonstrated repeatedly, including qEEG, event-related potentials (ERPs) and fMRI.

Specificity of effect for EBF has been shown in several respects, most importantly through the sham-treatment studies described above. Research has also shown that the degree of improvement in ADHD symptoms as well as the degree of change in neurophysiological indices is positively correlated with the degree to which the subject is able to learn to alter the EEG during the training sessions, strongly suggesting that observed improvements in functioning result from the specific action of feedback-guided learning during training [12].

Only one published study obtained results that may be interpreted as discrepant with the broad outlines of this body of research [13]. This was a multiple baseline study of seven ADHD subjects with staggered intervals of standard EBF and reinforcement of randomly chosen frequencies, changed every few sessions. Behavioral measures and a CPT were repeated after every interval. Of the seven subjects, two dropped out of

alternative approach to

addressing the primary

symptoms of the disorder

the study prior to completion.

Analyses based on those five subjects who completed the study show positive treatment effects for EBF of moderate-tolarge effect size. When the two drop-outs were included in the analyses, no significant EBF effects were found when controlling for linear trend. The authors acknowledge that one drop-out was a clear

outlier with negative response to active EBF treatment, but do not discuss possible reasons for this response, and conclude that the study failed to support the hypothesis of positive EBF effect. However, a number of significant methodological weaknesses call this conclusion into question, including poor operationalization of the placebo condition (which was in fact contingent feedback likely to have interfered with consolidation of learning in the treatment trials that always followed), failure to counterbalance condition, failure to exclude those subjects who did not show the pattern of cortical deactivation that EBF treatment is designed to treat and failure to measure success in learning to alter the EEG during EBF training sessions.

In assessing the evidence base for EBF, it is also important to remember that recent meta-analyses comparing the results of observational studies versus randomized controlled trials to assess efficacy of medical treatment reveal that results from the two approaches to research are generally concordant [14-16]. For example, analyzing data from 136 published reports of efficacy of 19 diverse medical treatments, Benson and Hartz concluded 'In only two of the 19 analyses of treatment effects did the combined magnitude of the effect from the observational studies lie outside of the 95% confidence interval for the combined

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magnitude in the randomized controlled trials' [14]. These findings suggest that a balanced approach to the status of scientific evidence should take into account results from observational as well as controlled trials in assessing the degree of empirical support for an intervention and call into question the empirical basis for the increasing tendency to accept as adequate evidence only results from randomized controlled trials. The latter bias appears itself to represent an opinion unsupported by the evidence base.

Nevertheless, it is also true that no double-blind, randomized-controlled trial has been completed to date that incorporates a large enough sample size to be considered definitive. Current standards of empirical evidence have developed to the point that no method is considered to have acquired conclusive empirical support in the absence of such a study. Unfortunately, this is an enormously expensive enterprise, which, practically speaking, could not be carried out without generous public support or private-sector support based on the expectation of a very substantial commercial market. However, as of yet, there has been no such public support and any substantial commercial benefit is highly unlikely, at least in the near term.

The body of research completed to date does appear to warrant funding of such a definitive study. In addition, further

research is needed to supplement initial studies of the durability of treatment effects attributed to EBF. Only two studies have been completed. One is a follow-up of a series of clinic patients interviewed by a blind rater using questions derived from established rating scales [17]. The second is a follow-up study of a controlled

trial in which the original subject pool was re-evaluated 1 and 3 years after EBF treatment ended [18]. Both studies showed significant maintenance of the treatment effect.

Finally, in considering the evidence base for EBF for ADHD, it is important to note that no lasting adverse effects have been reported in the research literature.

Several reviewers have emphasized the limitations of the extant research (prior to the DeBeus and Levesque studies) and concluded, simply, that EBF is 'unsupported' as a treatment for ADHD [19,20]. For a variety of reasons, however, such a simple, dichotomous view of the question is insufficient. In several areas of intervention, results from meta-analytic studies support the adoption of a more refined approach to evaluating efficacy [21]. Position papers and practice standards promulgated by the American Psychological Association [22] and the American Academy of Child and Adolescent Psychiatry [23] similarly argue in favor of an approach to assessing the degree of evidence that appreciates various levels or types of evidence, rather than restricting consideration to randomized controlled trials only or holding to a simple supported versus unsupported dichotomy.

I would also argue that the realities of everyday clinical experience require a more sophisticated and complex calculus. There are some uncomfortable realities regarding ADHD treatment that receive less attention than they deserve and that bear

critically on the question of the clinical utility of EBF and its place in an evidence-based practice. Numerous studies have shown that a substantial percentage (estimates range from 50 to 87%) of children and adolescents diagnosed with ADHD in the USA either do not begin, or fail to continue medical treatment [24,25]. The increased risk for a host of serious negative outcomes that is associated with untreated ADHD is well known [26].

In everyday clinical practice, a very high percentage of patients treated with EBF fall into one of two groups. Most numerous by far are patients who have tried medical treatment, most often with several trials of several agents, and have not benefited or not benefited enough, or have experienced adverse effects. Also in this group are individuals who have responded positively to medical treatment but would like to see if EBF can help them reduce their need for medication over the very long term, or enable them to stop medication entirely.

A second group are those who are determinedly opposed to such medical treatment and are looking at EBF as an alternative to medical treatment. In actual practice then, EBF is almost exclusively being used where first-line medical treatment is insufficient or is not in accord with the patients' preferences and values. This state of affairs is entirely appropriate, given the evi-

dence base. Indeed, I would argue that an informed approach to evidence-based practice with ADHD would fully and wholeheartedly recommend such a role for EBF in the treatment of ADHD. This view suggests that EBF is making an important clinical contribution in providing research-supported treatment to those who would otherwise remain untreated.

In addition, EBF offers the promise of eliminating or significantly reducing the need for regular medication use that is likely to be necessary for a lifetime for a high percentage of patients. In my experience, many parents express strong misgivings about this prospect. Finally, in practice, we often see significantly improved emotional regulation and lability and reduced anxiety. These changes are usually observed before changes in ADHD symptoms are evident. Parents will say something like "I'm not sure his attention is better yet, but he sure is easier to live with." In parallel with this, we often see improved parent—child relationships and reduced parent and familial stress.

Evidence-based practice has been defined as 'the integration of the best available research with clinical expertise in the context of patient characteristics, culture, and preferences' [27]. Given this definition and the research evidence summarized above, what then is the place of EBF in the practical realities of everyday clinical practice with ADHD? In my reading of the evidence, EBF is best viewed as an alternative approach to addressing the primary symptoms of the disorder that has substantial, but not yet conclusive, evidence of efficacy. It is quite time consuming and expensive and the process is often experienced as boring by patients (at least after an initial period of 'gee whiz' enthusiasm about the process.) There is preliminary evidence that any gains that may be obtained will

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last. It would appear to be well worth considering by patients when standard medical treatments fail or are insufficient, or when patient values and preferences lead to opposition to medical treatment. There is very little chance of harm, apart from the loss of time and money. There is probably more empirical evidence in support of EBF than for many of the off-label uses of medications or medication stacking that are often attempted when first-line treatments fail. EBF may be especially appropriate when medical treatment is contraindicated owing to cardiac or other considerations.

I have met with many patients from families that are determinedly opposed to medical treatment. If the untreated ADHD is resulting in serious negative consequence for the patient at the present time, I will often suggest to parents that they consider medical treatment as a short-term solution along with EBF for the longer term. I have also experienced patients whose parents decided to try medical treatment when EBF was not successful. In these instances, a trial of EBF allows patients to engage in medical treatment who might not otherwise have done so.

In my view, overall, a careful and pragmatic integration of the research evidence with the realities of clinical practice and patient preferences point unambiguously to acceptance of EBF as an evidence-based treatment that should always be considered as an option in discussing treatment possibilities with patients. This is in accordance with practice standards promulgated by the American Academy of Child and Adolescent Psychiatry for evaluating the evidence base of psychiatric treatments. EBF meets the standard of 'Clinical Guidelines' for ADHD owing to the presence of "limited empirical evidence (such as open trials, case studies) and/or strong clinical consensus." These practices should always be considered by the clinician but there are exceptions to their application [23].

A great deal of research on EBF remains to be carried out. However, this will be a long time in coming. In the meantime, EBF is best viewed as an evidence-based approach to the treatment for ADHD that offers an important option for consideration in the context of the values and preferences of each patient.

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