



The Brown University

Child & Adolescent Psychopharmacology

UPDATE

THE PREMIER MONTHLY FORUM ABOUT THE USE OF PSYCHOTROPIC MEDICATIONS IN THE YOUNG

ALTERNATIVE TREATMENTS

Experts review emerging brain-based interventions for children and adolescents

The authors of an interesting review article in the January issue of *Child and Adolescent Psychiatric Clinics of North America* urge that it is time to look more seriously at some bio-electric interventions for

précis

A review of evidence on three nonpharmaceutical technologies:

- **Electroencephalographic biofeedback:** various stimuli used to train patients to alter and normalize EEG patterns
- **Vagal nerve stimulation:** uses an implanted device to send electrical current to the vagal nerve
- **rTranscranial magnetic stimulation:** aims short pulses of magnetic energy at the various areas of the brain

treatment of mental illness, and that attention should include further research on these alternatives.

In an overview of three nonpharmaceutical technologies — electroencephalograph biofeedback (EBF), vagal nerve stimulation (VNS) and repetitive transcranial magnetic stimulation (rTMS) — Laurence Hirshberg, Ph.D., and colleagues contend that use of sophisticated technology to improve brain function is just beginning.

Noting the skepticism some of these methods arouse, Hirshberg says, “I think most typically these methods will be adjunctive to psychopharmacology and I don’t think that is likely to change in the near future.”

Nevertheless, he adds, “My wish for my child psychiatry colleagues is that they keep an open mind about this and that they look at the data.”

A key to the credibility of these unconventional interventions will be the revolution in neuroimaging that allows direct study of brain

function, Sufen Chiu, M.D., Ph.D., Assistant Professor at University of California, Davis and a co-author of the review, told *The Update*.

“People like to see a direct effect that they can measure in terms of how it is changing the body,” she says, and neuroimaging will make that possible for these technologies, as well as other interventions.

Their review does stress, however, that with these techniques, “In some instances, there is little experience to date with child and adolescent populations, requiring inferences about application to this population.”

One of these technology-based interventions, EEG biofeedback (EBF), has been used for 30 years, notes Hirshberg, who heads the NeuroDevelopment Center in Providence, Rhode Island. Hirshberg, who is also a Clinical Assistant Professor in the Department of Psychiatry and Human Behavior at Brown University, has worked extensively with EBF. But now studies with real time feedback from functional magnetic resonance imaging (fMRI) are beginning to replicate what EBF has indicated, allowing for the use of real-time information to alter and enhance brain function.

Most brain-based interventions are based on a belief that psychiatric symptoms may improve by altering inputs to the brain and modulating neuronal processing. For EBF, various stimuli (e.g., auditory, visual, tactile) can be used to train patients to alter and “normalize” EEG patterns.

“Basically,” says Hirshberg, “EBF induces change by simply showing the [patient] in real time what his or her brain is doing and providing instantaneous signals when it changes in the desired direction.”

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ALTERNATIVE TREATMENTS

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Evidence for EBF

Hirshberg argues that the evidence on EBF is strong and that interest in the field has picked up in the last five years. The studies, many of which have been done on ADHD have been done in both child and adult populations. According to the reviewers, these studies demonstrated that 70-80% of participants benefited from EBF and that the effect size may be somewhat equal to that of stimulants for the treatment of ADHD symptoms. (See Monastra review for data on ADHD.)

Studies on EBF have also shown improvements in attention, mood, anxiety, impulsivity, memory and learning as well as clinically significant improvements in addictive disorders and epilepsy in children and adults. (See Walker and Kozlowski review for data on epilepsy.)

The authors claim that the evidence for EBF treatment for several psychiatric disorders is at a level now that meets the American Academy of Child and Adolescent

Psychiatry's (AACAP) criteria for "Clinical Guidelines" (see Table 1, left). According to these AACAP criteria, an intervention meeting the "Clinical Guidelines" standard, which is the criteria that is met by stimulant medications for ADHD, would be expected to apply in clinical practice approximately 75% of the time.

Although the evidence is by far the most conclusive for ADHD, EBF also meets the "Clinical Guidelines" criteria for treatment of seizure disorders, anxiety disorders, depression, reading disabilities, and addictive disorders, according to the review article. (See Hammond review for data on anxiety and depression.)

"Specific recommendations, based on the body of empirical evidence available at present, suggest that EBF be considered by clinicians and parents as a first line treatment for ADHD when parents or patients prefer not to use medication and as an option in cases when significant side effects or insufficient improvement occurs with medication," the authors state. They also say that EBF might be a consideration for other disorders (e.g. anxiety, depression, and addictive disorders) when other treatment options are ineffectual, not well tolerated or contraindicated.

In addition, note the authors, there are clinical reports of EBF use for migraines, reactive attachment disorder and autistic spectrum disorder. The review also points out that, "EBF also may be used in combination with psychopharmacology or psychotherapy."

While they do point to an ample body of research, the authors caution that there are "significant methodological weaknesses in some of these studies and much fundamental research remains to be conducted."

The authors also note that, despite the advent of real time fMRI feedback, the use of EEG biofeedback is not likely to evaporate. Because fMRI equipment is much more expensive, it probably will not replace the EBF soon. That being the case, the researchers emphasize, it's important to do comparison studies between real time fMRI and EBF work.

Brain stimulation techniques

Whereas EBF is brain-based self-regulation, say the authors, the other two techniques they review are examples of brain stimulation.

Vagal nerve stimulation, approved by the FDA several years ago for epilepsy

treatment, uses a pacemaker-like implanted device to send a small electrical stimulation to the vagal nerve. Trial studies show it helps reduce epileptic seizures in various age groups, with an up to 44 percent reduction in adolescents at 18 months of continuous use. Studies have also shown some improvement for some patients using the device for depression.

Evidence for VNS use for epilepsy meets the standard for AACAP "Clinical Guidelines," meaning it should be considered for that disorder, say the authors. However, they indicate, until further research is done it can only be considered an "option" for refractory psychiatric disorders, meaning a practice that is "acceptable but not required." (See Martinez et al. review for data on VNS.)

The other technique reviewed, repetitive transcranial magnetic stimulation (rTMS), in which short pulses of magnetic energy repeated at intervals are aimed at the brain to stimulate nerve cells over a number of clinical sessions, is not approved by the FDA, note the researchers. But it is being investigated for a number of mental disorders including major depression and anxiety. Case studies have reported improvements in children with unipolar disorder, bipolar disorder and schizophrenia. The authors say the small number of case reports for rTMS indicates it might be considered as a treatment option for these problems, under AACAP standards, but only where medications have not worked. (See Morales et al. review for data on rTMS.)

In addition to the evidence on these individual technologies, some clinical experience indicates that combining biofeedback and brain stimulation may be more effective than either intervention alone, say the authors. For example, there is work using visual, auditory or magnetic stimulation to assist in biofeedback training.

The authors call for more research into all three of these techniques for psychiatric disorders in children, using large randomized, double-blind placebo controlled trials. At the same time they note that it will be difficult to do that type of conventional research with these interventions. For example, people using biofeedback quickly recognize whether or not the signals are reflecting what is happening with them, making a double-blind situation extremely difficult.

That's why, argue the authors, it will be

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Table 1 AACAP guidelines for recommending evidence-based treatments

•"Minimal Standards"

are recommendations that are based on substantial empirical evidence (such as well-controlled, double-blind trials) or overwhelming clinical consensus. Minimal standards are expected to apply more than 95% of the time. i.e., in almost all cases. When the practitioner does not follow this standard in a particular case, the medical record should indicate the reason.

•"Clinical Guidelines"

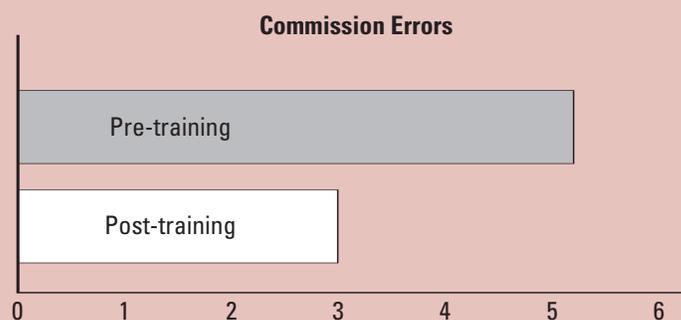
are recommendations that are based on limited empirical evidence (such as open trials, case studies) and/or strong clinical consensus. Clinical guidelines apply approximately 75% of the time. These practices should always be considered by the clinician, but there are exceptions to their applications.

Data from Greenhill LL, Pliszka D, Dulcan MK, et al.: Practice parameter for the use of stimulant medications in the treatment of children, adolescents, and adults. *J Am Acad Child Adolesc Psychiatry* 2002; 41(2 Suppl):26S-49S.

Can neurofeedback training improve attention?

The neurofeedback training in the study illustrated below involved training the subjects to enhance beta waves (both sensorimotor rhythm [SMR] and beta1). A reduction in both of these frequencies has been associated with some ADHD symptoms, including inattention and over-activity. Some researchers think that targeting and enhancing these frequencies may improve attentiveness, which could help children with ADHD.

The graph shows changes in healthy subjects' performance on the test of variables of attention (TOVA) measure of continuous performance after 10 neurofeedback training sessions. This is a well-validated computerized test of inattention (reflected in omission errors, where subjects failed to respond to a target stimulus) and impulsivity (reflected in commission errors, where subjects erroneously responded to a non-target stimulus). The data show fewer impulsive errors on the TOVA after neurofeedback training, indicating that cognitive performance may have been affected.



Data from Figure 1 in Gruzelier J, Egner T: Critical validation studies of neurofeedback. *Child Adolesc Psychiatr Clin N Am* 2005 Jan; 14(1):83-104.

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necessary to develop new research models to validate these practices.

Despite the many barriers that any unconventional intervention faces, particularly in mental health, circumstances may have created opportunity for these techniques, says Chiu: "I think we are at a very important time. There is a real heightened awareness to the risk of using medications, particularly for children."

Even though we don't know everything about the risks of these alternatives either, she says, "At least we can consider other interventions." ■

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Hirshberg LM, Chiu S, Frazier JA: Emerging brain-based interventions for children and adolescents: overview and clinical perspective. *Child Adolesc Psychiatr Clin N Am* 2005; 14:1-19. E-mail: lhirshberg@neurodevelopmentcenter.com, lhirshberg@cox.net.

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