CME Article

Electroencephalogram Neurofeedback: Application in ADHD and Epilepsy

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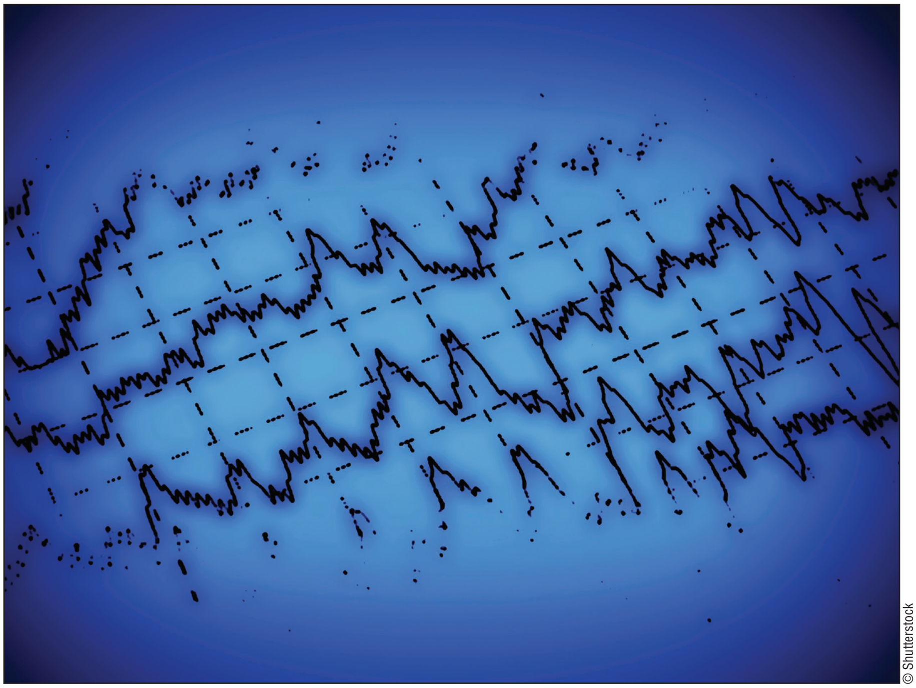
ABSTRACT

The use of electroencephalogram neurofeedback has been studied in a number of psychiatric disorders, especially for the treatment of attention-deficit/hyperactivity disorder (ADHD). However, many clinicians are not aware of this treatment and the level of evidence supporting its use. In this article, we review the evidence for the efficacy of neurofeedback in several psychiatric disorders and also discuss the specific neurofeedback protocols that have been found effective in the treatment of ADHD, such as slow cortical potential, theta/beta ratio, and sensorimotor rhythm neurofeedback. **[*Psychiatr Ann.* 2016;46(10):594-600.]**



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Neurofeedback is a behavioral therapy technique used to teach or improve self-regulation of brain activity. It is a variant of electroencephalogram (EEG) biofeedback, which aims to help the patient acquire self-regulation over certain brain activity patterns based on operant conditioning principles.[1,2] The EEG shows electrical activity of the cerebral cortex and reflects the summation of synchronized excitatory and inhibitory postsynaptic potentials of apical cortical pyramidal cells. The roots of neurofeedback can be traced back to the early 1930s, when the first observations were made that the EEG alpha-blocking response could be classically conditioned.[3,4] EEG was more systematically investigated and its efficacy confirmed in the 1940s.[5,6] These early studies clearly demonstrated that conditioning principles can be applied to EEG parameters such as the alpha-blocking response.

The first successful application of EEG conditioning with clinical effects, namely anticonvulsant effects, was reported in 1968 by Wyrwicka and

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Sterman.[7] This work involved the training of the sensorimotor rhythm (SMR) in cats. This EEG rhythm was previously associated with stereotyped postures characterized by a complete cessation of spontaneous activity and immobile behavior in the cat.[7] Furthermore, training of this EEG rhythm during wakefulness resulted in increased sleep spindle density during sleep (an EEG rhythm with the same frequency and topographical distribution as SMR) and improved sleep quality in cats,[8] a finding that was also replicated in humans.[9,10] In a serendipitous finding, the anticonvulsant effects of operant conditioning of this SMR rhythm in cats exposed to the convulsant drug monomethylhydrazine were demonstrated,[11] followed by replications of these effects in humans.[12] These initial findings resulted in what we currently know as "frequency band neurofeedback." About the same time, the first report of voluntary control over a slow brain potential called the contingent negative variation or "bereitschaftspotential" (readiness potential, due to the property of this potential to emerge when preparing for action, such as when waiting at a traffic light) was reported,[13] which laid the foundation of another well-known neurofeedback approach—slow cortical potential (SCP) neurofeedback.

Frequency band neurofeedback targets abnormal activity in frequency bands, such as high or low power in a specific frequency band or in a ratio of two frequency bands. For attention-deficit hyperactivity disorder (ADHD), this might be a high theta/beta ratio or high theta power and/or low beta power in children,[14] and similar patterns in adults.[15-17] The goal of frequency band neurofeedback is to activate a specific brain network, which is achieved by changing the amplitude of a specific frequency band. To do so, a therapist either selects the target frequency band according to the individual quantitative EEG or employs standard protocols. For ADHD, a standard protocol might be the up-training of the SMR (12-15 Hz) or a down-training of the theta/beta ratio (4-7 Hz/13-21 Hz),[2] and for epilepsy this might be an SMR up-training with concurrent theta down-training.[12] Standard protocols are based on group-average findings that might not hold for the individual patient; therefore, some level of personalization of neurofeedback could enhance treatment outcome.[18,19]

> ***The goal of frequency band neurofeedback is to activate a specific brain network.***

SCP neurofeedback is focused on learned self-regulation of cortical activation and inhibition. These threshold-regulation mechanisms are slow electrical shifts in brain activity. They change periodically from being electrically positive to electrically negative and are described as a phasic tuning mechanism in the regulation of attention.[20] They are generated cortically and subcortically, involving brain stem reticular mechanisms, the thalamus, and the basal ganglia. The main factor contributing to SCP is synaptic activities at apical dendrites in superficial layers of the cortex. Negativation (ie, the signal becoming electrically negative) represents activation, increasing the firing probabilities of the underlying cortical areas, and is caused by long-lasting depolarization of superficial layer apical dendrites. Positivation represents an inhibition and a decrease in firing probabilities. SCPs are related to cognitive performance and motor actions. A positive shift reflects consumption of resources and disfacilitation of excitation thresholds. A negative shift reflects provision of resources and facilitates attention as well as initiation of goal-directed behavior that can be observed in enhanced reaction time, stimulus detection, and short-term memory during the negative shift phase.[21] In SCP neurofeedback, both conditions are trained (activation/negativation and deactivation/positivation). Self-regulation of SCPs is important in disorders with impaired excitation thresholds, such as epilepsy or ADHD.

Both types of neurofeedback (ie, frequency band neurofeedback and SCP neurofeedback) were originally employed in the treatment of epilepsy,[22] but are now also used in the treatment of ADHD. Both ADHD and epilepsy are characterized by difficulties in regulation of cortical excitation thresholds. A meta-analysis of the efficacy of frequency (especially SMR) and SCP feedback treatment in ADHD reported clinical effects with a large effect size (ES) on inattention and impulsivity and a medium ES on hyperactivity.[23]

Neurofeedback has been used for several disorders such as ADHD, epilepsy, migraine, depression, autism, tinnitus, anxiety, and others, but the only evidence-based applications for this technique are for ADHD and epilepsy. Neurofeedback might be beneficial for other disorders, but the body of research is too small to make any valid claims.

ADHD

Several years after Sterman and Friar's[24] initial demonstration of the anticonvulsant effects of SMR neurofeedback, Lubar and Shouse[25] described the application of this same SMR neurofeedback in a child with hyperkinetic disorder. Employing an A-B-A design, they reported improvements in hyperactivity and distractibility when SMR was up-trained and found that symptoms worsened when reversal training was used.[25] A few years later, these findings were subsequently replicated in a larger study.[26] These reports can now be considered the first demonstrations of clinical effects after neurofeedback in what we today refer to as ADHD.

The first two randomized controlled trials (RCTs) compared neurofeedback to a waiting-list control group and found improvements in attention and hyperactivity.[27,28] More recently, four RCTs have been published either using a cognitive training-based[29-31] or an electromyogram (EMG)-based biofeedback training[32] as a control condition. These control conditions were aimed at controlling for nonspecific effects of neurofeedback, such as the time of computer interaction and amount of client-therapist interaction. Another RCT compared SCP with theta/beta ratio neurofeedback, and found similar effects for both treatments on ADHD symptoms.[33]

In all of the RCT studies except that by Holtmann et al.,[30] neurofeedback training effects were greater than the control condition with respect to ADHD symptoms (typically a medium ES) according to parent and teacher ratings. In three of these RCTs, follow up was performed and the clinical effects were maintained at the 6-month[34] and 2-year follow-up visits.[35] Two of these RCTs were multicenter studies with large sample sizes (n = 102[36] and n = 104[37]).

In the past few years, several reviews[38-46] and meta-analyses[18,23,47] on ADHD investigated the effectiveness of nonpharmacologic treatments, especially neurofeedback, for ADHD. In general, all reviews and meta-analyses found positive effects of neurofeedback for ADHD as rated by parents. They agreed that neurofeedback is as effective or more effective than waiting-list groups, computerized cognitive training, and EMG feedback. The largest effect sizes were found for improvements in symptoms of inattention (>0.8) and impulsivity (>0.6), with smaller effect sizes for hyperactivity (>0.3).[23] Two RCTs found that neurofeedback was not inferior to treatment with psychostimulants.[48,49] Some investigations concluded that neurofeedback is an "efficacious and specific" treatment for ADHD,[23,38] and some still see a need for methodologically improved studies.[44,47] Additionally, some clinical trials are in the process of publication and preliminary results are promising regarding quality of study design as well as clinical outcome.[50,51]

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In addition to behavioral and clinical improvements, other improvements have also been reported, including faster reaction times, smaller reaction time variability, and reduced error rates.[52-54] Improvements in brain activity have also been reported, such as improved contingent-negative variation and event-related potentials (brain activity patterns that reflect preparation and attention) in children[18,30,52,55,56] and adults,[57] as well as improvement in EEG frequency bands.[32,58] One study investigated the effects of neurofeedback on sleep in children and adults with ADHD and found improved sleep-onset latency and sleep quality after SMR neurofeedback that also mediated the clinical effects of inattention.[59] Furthermore, functional magnetic resonance imaging studies were able to demonstrate structural changes after neurofeedback in healthy participants[60] and in patients with ADHD.[61] These findings provide further support for understanding the underlying mechanism of neurofeedback and its efficacy. The underlying mechanisms of action have also been investigated in theoretical articles[2,62] and via studies that apply neurofeedback to healthy participants to investigate the effect on neurophysiologic mechanisms and changes.[63,64] Details of these studies are not described here, but these studies show that research interest is ongoing as neurofeedback yields such positive and promising results.

However, some of the studies and the reviews and even the meta-analyses themselves have been criticized for methodologic failures and shortcomings. Shortcomings in the design and procedure of neurofeedback studies are the main problems in proving its effectiveness. Aside from the fact that the gold standard of placebo-controlled, randomized, double-blind studies cannot be easily achieved in neurofeedback therapy,[2] there are methodologic failures in some of the studies conducted. Studies that did not find clinically significant effects of neurofeedback all had several features in common, such as the use of unconventional neurofeedback protocols and feedback locations,[65-71] substantial deviations from the pre-registered clinical trials register (such as only including 60%[70,72] to 34%[68] of the pre-registered sample size) and the use of suboptimal methodology to optimize learning (eg, game-like implementations[2]). Note that in regard to learning principles, if a feedback animation is too exciting and thrilling, it might create a stimulus-reinforcer association instead of a response-reinforcer association, which means that the participants will associate the reinforcement with the stimulus rather than the desired brain activity.[73] Furthermore, motivation and reinforcement need to be given by the therapist, which makes double-blind, placebo-controlled studies especially hard to implement.

The problems mentioned regarding the studies with no clinical effects were further highlighted in a recent meta-analysis that found overall effects of neurofeedback in ADHD when inspecting parent ratings, but not significant effects for teacher ratings.[74] However, when limiting to neurofeedback studies that used "standard" protocols, there were significant clinical benefits for both parent-rated and teacher-rated symptoms.[74] Currently, some large multicenter, controlled studies are being conducted[75] or in the process of being published.[50]

From recent conferences it can be concluded that (at least in the completed study[50]) a large sample size and well-designed control conditions yield promising results supporting the efficaciousness of neurofeedback. Taken together, neurofeedback can be deemed a viable treatment option for ADHD that is efficacious and specific.

EPILEPSY

Epilepsy is not an official psychiatric disorder but has the second-best evidence in neurofeedback research and is therefore described here.

Early studies employing SMR neurofeedback, such as those by Sterman et al.,[76] Lubar and Bahler,[77] and later studies employing SCP neurofeedback from the 1990s[22,78,79] and early 2000s[80] all showed promising anticonvulsant effects in epilepsy. The mechanisms of action are thought to be related to the ability to regulate brain excitation thresholds and therefore prevent over-excitation and a subsequent seizure. Studies from two independent research groups examined this and delivered promising clinical results (for review and meta-analysis see Tan et al.[12]). SMR and SCP neurofeedback protocols proved to be the most effective in the treatment of epilepsy with focal seizures. However, in the 2000s, this research interest decreased dramatically, with only three results in the literature search for the past 7 years (one review,[81] one meta-analysis,[12] and one follow-up study[82]). The meta-analysis by Tan et al.[12] and the review by Nagai[81] concluded that neurofeedback was found to produce a significant reduction in seizure frequency. The recent follow-up study was able to demonstrate that clinical effects were maintained even 10 years after treatment,[82] as seizure frequency was still reduced and the ability to regulate brain activity was still present. Given that the patient group consisted mostly of treatment-resistant patients, these results are encouraging and clinically meaningful.

OTHERS DISORDERS

Several studies[83,84] have also reported on the effect of neurofeedback in other disorders, but only a few controlled and randomized studies[83,84] have been conducted for other indications. Therefore, although some indications appear promising, more research is needed to reach solid conclusions for the efficacy of neurofeedback in disorders other than ADHD and epilepsy.

LONG-TERM EFFECTS AND CURRENT POSITION OF NEUROFEEDBACK

Currently, the gold standard of treatment for ADHD is psychostimulant medication, including methylphenidate and various amphetamine formulations with large effect sizes on the group level in the acute treatment of ADHD.[85] However, the clinical efficacy of psychostimulant medication decreases over time, as demonstrated in various large-scale studies,[86,87] possibly related to an up-regulation of dopamine transporter availability after sustained treatment.[88] Therefore, the need for more effective and longer-lasting treatments in ADHD is widely accepted. Because neurofeedback is based on operant conditioning principles, once the regulation of the brain is learned and the treatment was effective, these effects are thought to be permanent. Interestingly, some subsequent studies have all shown that clinical benefits were maintained or even further improved at the 6 month follow-up[34,37,53] and even after 2 years.[35] Interestingly, patients were still able to regulate their brain activity in the desired direction at these follow-up moments.[35,53] The same is true for patients with epilepsy in a 10-year follow-up study.[82] Additionally, neurofeedback does not have any severe side effects.[67,68]

NEUROFEEDBACK IS NOT "MAGIC IN A BOX"

Neurofeedback is part of behavioral psychotherapy and should be applied according to those standards. A positive neurofeedback treatment should be based on individual brain activity, learning principles, a good patient-therapist relationship, motivational components, and possibly accompanying traditional psychotherapy. Neurofeedback should be accompanied by additional behavioral therapy components implied in the sessions. Most SCP neurofeedback studies with children always implement a token system and transfer to daily-life situations. The study by Drechsler et al.[54] used extended support from the parents for the daily transfer; all other studies[53] kept the parents rather uninvolved. The transfer into daily life can range from handing out transfer cards and the instruction to practice regulation at home, to sitting down and guiding the children into an activated state during their homework or other tasks. This component seems to be an important tool for application of the learned self-regulation into daily life, be it monitored by parents or by the children on their own.

SELF-DIRECTED EEG NEUROFEEDBACK USING WEARABLE DEVICES

During the past few years, there has been development of "home training devices" or "self-directed neurofeedback" for several reasons, such as the many sessions that are required, travel time, the availability of the therapist, and reduction of costs. To this date, there are no systematic studies that we are aware of on the effect of neurofeedback home-training for psychiatric disorders. Such unsupervised "home training" also implicates that the feedback process that is currently performed by a trained clinician can be fully and effectively automated. As indicated above, some of the double-blind studies (implicating that all parties, including the therapist, were blinded) necessitated automated feedback procedures; however, all such studies have been found ineffective,[66,89,90] making it difficult to expect that such an automated approach is feasible at this moment. This will require more research and validation. Therefore, in the near future, it will be more likely that such home-training approaches will consist of "supervised home training" in which the therapist can access the feedback tools remotely and apply the neurofeedback remotely, sometimes termed "tele-neurofeedback."

In addition to the development of home training, there has also been large growth in "neuro-devices" claiming to provide all kinds of sophisticated feedback, supposedly based on brain activity. In our view, these devices cannot be recommended for the following reasons: (1) the signal quality is low, (2) they are not medically certified, (3) the electrophysiologic foundations are unclear, (4) the application is unsupervised, and (5) they do not have any published data to support their efficacy. At this stage, the only possible home-training option is tele-neurofeedback with direct supervision by the therapist via remote access to computers and devices. Previous caregiver and neurofeedback training by the therapist is advised.

CONCLUSION

Overall, it can be concluded that psychiatrists can recommend neurofeedback to patients with ADHD as an effective treatment when standard protocols, such as SMR, SCP, and theta/beta neurofeedback, are used. However, one should remain cautious regarding the use of neurofeedback for other indications due to a lack of sufficient evidence. Even if some neurofeedback providers sell their product with different claims, therapists should be aware of the evidence base and look critically at the quality of the product as well as its claim. Neurofeedback is an excellent tool for training certain brain networks and therefore improving behavior, but the therapist is still an indispensable component in the treatment.

REFERENCES

1. Sherlin L, Arns M, Lubar J, et al. Neurofeedback and basic learning theory: implications for research and practice. *J Neurother*. 2011;15(4):292-304.
2. Arns M, Heinrich H, Strehl U. Evaluation of neurofeedback in ADHD: the long and winding road. *Biol Psychol*. 2014;95:108-115.
3. Durup G, Fessard AI. L'électrencéphalogramme de l'homme. Observations psycho-physiologiques relatives à l'action des stimuli visuels et auditifs. *L'année Psychologique*. 1935;36(1):1-32.
4. Loomis AL, Harvey EN, Hobart G. Potential rhythms of the cerebral cortex during sleep. *Science*. 1935;81(2111):597-598.
5. Jasper H, Shagass C. Conditioning the occipital alpha rhythm in man. *J Exp Psychol*. 1941;28(5):373-387.
6. Knott JR, Henry CE. The conditioning of the blocking of the alpha rhythm of the human electroencephalogram. *J Exp Psychol*. 1941;28(2):134-144.
7. Wyrwicka W, Sterman MB. Instrumental conditioning of sensorimotor cortex EEG spindles in the waking cat. *Physiol Behav*. 1968;3(5):703-707.
8. Sterman MB, Howe RC, Macdonald LR. Facilitation of spindle-burst sleep by conditioning of electroencephalographic activity while awake. *Science*. 1970;167(921):1146-1148.
9. Hoedlmoser K, Pecherstorfer T, Gruber G, et al. Instrumental conditioning of human sensorimotor rhythm (12-15 Hz) and its impact on sleep as well as declarative learning. *Sleep*. 2008;31(10):1401-1408.
10. Schabus M, Heib DP, Lechinger J, et al. Enhancing sleep quality and memory in insomnia using instrumental sensorimotor rhythm conditioning. *Biol Psychol*. 2014;95:126-134.
11. Sterman B, Lopresti RW, Fairchild MD. Electroencephalographic and behavioral studies of monomethylhydrazine toxicity in the cat. *J Neurother*. 2010;14(4):293-300.
12. Tan G, Thornby J, Hammond DC, et al. Meta-analysis of EEG biofeedback in treating epilepsy. *Clin EEG Neurosci.* 2009;40(3):173-179.
13. McAdam DW, Irwin DA, Rebert CS, Knott JR. Conative control of the contingent negative variation. *Electroencephalogr Clin Neurophysiol*. 1966;21(2):194-195.
14. Barry RJ, Clarke AR, Johnstone SJ. A review of electrophysiology in attention-deficit/hyperactivity disorder: I. Qualitative and quantitative electroencephalography. *Clin Neurophysiol*. 2003;114(2):171-183.
15. Bresnahan SM, Anderson JW, Barry RJ. Age-related changes in quantitative EEG in attention-deficit/hyperactivity disorder. *Biol Psychiatry*. 1999;46(12):1690-1697.
16. Bresnahan SM, Barry RJ. Specificity of quantitative EEG analysis in adults with attention deficit hyperactivity disorder. *Psychiatry Res*. 2002;112(2):133-144.
17. Clarke AR, Barry RJ, Heaven PC, McCarthy R, Selikowitz M, Byrne MK. EEG in adults with attention-deficit/hyperactivity disorder. *Int J Psychophysiol*. 2008;70(3):176-183.
18. Arns M, Drinkenburg W, Kenemans JL. The effects of QEEG-informed neurofeedback in ADHD: an open-label pilot study. *Appl Psychophysiol Biofeedback*. 2012;37(3):171-180.
19. Monastra VJ, Monastra DM, George S. The effects of stimulant therapy, EEG biofeedback, and parenting style on the primary symptoms of attention-deficit/hyperactivity disorder. *Appl Psychophysiol Biofeedback*. 2002;27(4):231-249.
20. Rockstroh B, Elbert T, Birbaumer N, Lutzenberger W. Biofeedback-produced hemispheric asymmetry of slow cortical potentials and its behavioural effects. *Int J*

Psychophysiol. 1990;9(2):151-165.
21. Birbaumer N, Elbert T, Canavan AG, Rockstroh B. Slow potentials of the cerebral cortex and behavior. *Physiologic Rev*. 1990;70(1):1-41.
22. Rockstroh B, Elbert T, Birbaumer N, et al. Cortical self-regulation in patients with epilepsies. *Epilepsy Res*. 1993;14(1):63-72.
23. Arns M, de Ridder S, Strehl U, Breteler M, Coenen A. Efficacy of neurofeedback treatment in ADHD: the effects on inattention, impulsivity and hyperactivity: a meta-analysis. *Clin EEG Neurosci*. 2009;40(3):180-189.
24. Sterman MB, Friar L. Suppression of seizures in an epileptic following sensorimotor EEG feedback training. *Electroencephalogr Clin Neurophysiol*. 1972;33(1):89-95.
25. Lubar JF, Shouse MN. EEG and behavioral changes in a hyperkinetic child concurrent with training of the sensorimotor rhythm (SMR): a preliminary report. *Biofeedback Self Regul.* 1976;1(3):293-306.
26. Shouse MN, Lubar JF. Operant conditioning of EEG rhythms and ritalin in the treatment of hyperkinesis. *Biofeedback Self Regul.* 1979;4(4):299-312.
27. Lévesque J, Beauregard M, Mensour B. Effect of neurofeedback training on the neural substrates of selective attention in children with attention-deficit/hyperactivity disorder: a functional magnetic resonance imaging study. *Neurosci Lett.* 2006;394(3):216-221.
28. Linden M, Habib T, Radojevic V. A controlled study of the effects of EEG biofeedback on cognition and behavior of children with attention deficit disorder and learning disabilities. *Biofeedback Self Regul*. 1996;21(1):35-49.
29. Gevensleben H, Holl B, Albrecht B, et al. Is neurofeedback an efficacious treatment for ADHD? A randomised controlled clinical trial. *J Child Psychol Psychiatry*. 2009;50(7):780-789.
30. Holtmann M, Grasmann D, Cionek-Szpak E, et al. Spezifische wirksamkeit von neurofeedback auf die impulsivitӓt bei ADHS. *Kindheit und Entwicklung*. 2009;18(2):95-204.
31. Steiner NJ, Sheldrick RC, Gotthelf D, Perrin EC. Computer-based attention training in the schools for children with attention deficit/hyperactivity disorder: a preliminary trial. *Clin Pediatr* (Phila). 2011;50(7):615-622.
32. Bakhshayesh AR, Hänsch S, Wyschkon A, Rezai MJ, Esser G. Neurofeedback in ADHD: a single-blind randomized controlled trial. *Eur Child Adolesc Psychiatry*. 2011;20(9):481-491.
33. Leins U, Goth G, Hinterberger T, Klinger C, Rumpf N, Strehl U. Neurofeedback for children with ADHD: a comparison of SCP and theta/beta protocols. *Appl Psychophysiol Biofeedback*. 2007;32(2):73-88.
34. Gevensleben H, Holl B, Albrecht B, et al. Neurofeedback training in children with ADHD: 6-month follow-up of a randomised controlled trial. *Eur Child Adolesc Psychiatry*. 2010;19(9):715-724.
35. Gani C, Birbaumer N, Strehl U. Long term effects after feedback of slow cortical potentials and of theta-beta-amplitudes in children with attentiondeficit/hyperactivity disorder (ADHD). *Int J Bioelectromagn*. 2008;10(4):209-232.
36. Gevensleben H, Holl B, Albrecht B, et al. Is neurofeedback an efficacious treatment for ADHD? A randomised controlled clinical trial. *J Child Psychol Psychiatry*. 2009;50(7):780-789.
37. Steiner NJ, Frenette EC, Rene KM, Brennan RT, Perrin EC. In-school neurofeedback training for adhd: sustained improvements from a randomized control trial. *Pediatrics*. 2014;133(3):483-492.
38. Gevensleben H, Rothenberger A, Moll GH, Heinrich H. Neurofeedback in children with ADHD: validation and challenges. *Expert Rev Neurother*. 2012;12(4):447-460.
39. Gevensleben H, Kleemeyer M, Rothenberger LG, et al. Neurofeedback in ADHD: further pieces of the puzzle. *Brain Topogr*. 2014;27(1):20-32.
40. Moriyama TS, Polanczyk G, Caye A, Banaschewski T, Brandeis D, Rohde LA. Evidence-based information on the clinical use of neurofeedback for ADHD. *Neurotherapeutics*. 2012;9(3):588-598.
41. Mayer K, Wyckoff SN, Strehl U. One size fits all? Slow cortical potentials neurofeedback: a review. *J Atten Disord*. 2013;17(5):393-409.
42. Gruzelier JH. EEG-neurofeedback for optimising performance. I: a review of cognitive and affective outcome in healthy participants. *Neurosci Biobehav Rev*. 2014;44:124-141.
43. Hodgson K, Hutchinson AD, Denson L. Nonpharmacological treatments for ADHD: a meta-analytic review. *J Atten Disord.* 2014;18(4):275-282.
44. Holtmann M, Sonuga-Barke E, Cortese S, Brandeis D. Neurofeedback for ADHD: a review of current evidence. *Child Adolesc Psychiatr Clin N Am*. 2014;23(4):789-806.
45. Windthorst P, Veit R, Enck P, Smolka R, Zipfel S, Teufel M. Biofeedback and neurofeedback: applications in psychosomatic medicine and psychotherapy. *Psychother Psychosom Med Psychol*. 2015;65(3-4):146-158.
46. Zuberer A, Brandeis D, Drechsler R. Are treatment effects of neurofeedback training in children with ADHD related to the successful regulation of brain activity? A review on the learning of regulation of brain activity and a contribution to the discussion on specificity. *Front Hum Neurosci*. 2015;9:135.
47. Sonuga-Barke EJ, Brandeis D, Cortese S, et al.; European ADHD Guidelines Group. Nonpharmacological interventions for ADHD: systematic review and meta-analyses of randomized controlled trials of dietary and psychological treatments. *Am J Psychiatry*. 2013;170(3):275-289.
48. Duric NS, Assmus J, Gundersen DI, Elgen IB. Neurofeedback for the treatment of children and adolescents with ADHD: a randomized and controlled clinical trial using parental reports. *BMC Psychiatry*. 2012;12(1):107.
49. Meisel V, Servera M, Garcia-Banda G, Cardo E, Moreno I. Neurofeedback and standard pharmacological intervention in ADHD: a randomized controlled trial with six-month follow-up. *Biol Psychol*. 2013;94(1):12-21.
50. Holtmann M, Pniewski B, Wachtlin D, Wörz S, Strehl U. Neurofeedback in children with attention-deficit/hyperactivity disorder (ADHD)--a controlled multicenter study of a non-pharmacological treatment approach. *BMC Pediatr*. 2014;14:202.
51. Mayer K, Blume F, Wyckoff SN, Brokmeier LL, Strehl U. Neurofeedback of slow cortical potentials as a treatment for adults with attention deficit-/hyperactivity disorder. *Clin Neurophysiol.* 2016;127(2):1374-1386.
52. Heinrich H, Gevensleben H, Freisleder FJ, Moll GH, Rothenberger A. Training of slow cortical potentials in attention-deficit/hyperactivity disorder: evidence for positive behavioral and neurophysiological effects. *Biol Psychiatry*. 2004;55(7):772-775.
53. Strehl U, Leins U, Goth G, Klinger C, Hinterberger T, Birbaumer N. Self-regulation of slow cortical potentials: a new treatment for children with attention-deficit/hyperactivity disorder. *Pediatrics*. 2006;118(5):e1530-1540.
54. Drechsler R, Straub M, Doehnert M, Heinrich H, Steinhausen HC, Brandeis D. Controlled evaluation of a neurofeedback training of slow cortical potentials in children with Attention Deficit/Hyperactivity Disorder (ADHD). *Behav Brain Funct*. 2007;3:35.
55. Kropotov JD, Grin-Yatsenko VA, Ponomarev VA, Chutko LS, Yakovenko EA, Nikishena IS. ERPs correlates of EEG relative beta training in ADHD children. *Int J Psychophysiol.* 2005;55(1):23-34.
56. Wangler S, Gevensleben H, Albrecht B, et al. Neurofeedback in children with ADHD: specific event-related potential findings of a randomized controlled trial. *Clin Neurophysiol.* 2011;122(5):942-950.
57. Mayer K, Blume F, Wyckoff SN, Brokmeier LL, Strehl U. Neurofeedback of slow cortical potentials as a treatment for adults with Attention-Deficit/Hyperactivity Disorder. *Clin Neurophysiol*. 2016;127(2):1374-1386.
58. Gevensleben H, Holl B, Albrecht B, et al. Distinct EEG effects related to neurofeedback training in children with ADHD: a randomized controlled trial. *Int J Psychophysiol*. 2009;74(2):149-157.
59. Arns M, Feddema I, Kenemans JL. Differential effects of theta/beta and SMR neurofeedback in ADHD on sleep onset latency. *Front*

Hum Neurosci. 2014;8:1019.
60. Ghaziri J, Tucholka A, Larue V, et al. Neurofeedback training induces changes in white and gray matter. *Clin EEG Neurosci*. 2013;44(4):265-272.
61. Beauregard M, Lévesque J. Functional magnetic resonance imaging investigation of the effects of neurofeedback training on the neural bases of selective attention and response inhibition in children with attention-deficit/hyperactivity disorder. *Appl Psychophysiol Biofeedback*. 2006;31(1):3-20.
62. Ros T, J Baars B, Lanius RA, Vuilleumier P. Tuning pathological brain oscillations with neurofeedback: a systems neuroscience framework. *Front Hum Neurosci*. 2014;8:1008.
63. Gevensleben H, Moll GH, Rothenberger A, Heinrich H. Neurofeedback in attention-deficit/hyperactivity disorder - different models, different ways of application. *Front Hum Neurosci*. 2014;8:846.
64. Studer P, Kratz O, Gevensleben H, et al. Slow cortical potential and theta/beta neurofeedback training in adults: effects on attentional processes and motor system excitability. *Front Hum Neurosci*. 2014;8:555.
65. Ogrim G, Hestad KA, Kropotov J, et al. Predicting the clinical outcome of stimulant medication in pediatric attention-deficit/hyperactivity disorder: data from quantitative electroencephalography, event-related potentials, and a go/no-go test. *Neuropsychiatr Dis Treat*. 2014;10:231-242.
66. Lansbergen MM, van Dongen-Boomsma M, Buitelaar JK, Slaats-Willemse D. ADHD and EEG-neurofeedback: a double-blind randomized placebo-controlled feasibility study. *J Neural Transm*. 2011;118(2):275-284.
67. Arnold LE, Lofthouse N, Hersch S, et al. EEG neurofeedback for ADHD: double-blind sham-controlled randomized pilot feasibility trial. *J Atten Disord*. 2013;17(5):410-419.
68. van Dongen-Boomsma M, Vollebregt MA, Slaats-Willemse D, Buitelaar JK. A randomized placebo-controlled trial of electroencephalographic (EEG) neurofeedback in children with attention-deficit/hyperactivity disorder. *J Clin Psychiatry*. 2013;74(8):821-827.
69. Vollebregt MA, van Dongen-Boomsma M, Buitelaar JK, Slaats-Willemse D. Does EEG-neurofeedback improve neurocognitive functioning in children with attention-deficit/hyperactivity disorder? A systematic review and a double-blind placebo-controlled study. *J Child Psychol Psychiatry*. 2014;55(5):460-472.
70. Bink M, van Nieuwenhuizen C, Popma A, Bongers IL, van Boxtel GJ. Behavioral effects of neurofeedback in adolescents with ADHD: a randomized controlled trial. *Eur Child Adolesc Psychiatry*. 2015;24(9):1035-1048.
71. Maurizio S, Liechti MD, Heinrich H, et al. Comparing tomographic EEG neurofeedback and EMG biofeedback in children with attention-deficit/hyperactivity disorder. *Biol Psychol*. 2014;95:31-44.
72. Janssen TW, Bink M, Geladé K, van Mourik R, Maras A, Oosterlaan J. A randomized controlled trial investigating the effects of neurofeedback, methylphenidate, and physical activity on event-related potentials in children with attention-deficit/hyperactivity disorder. *J Child Adolesc Psychopharmacol*. 2016;26(4):344-353.
73. Sherlin L, Arns M, Lubar J, et al. Neurofeedback and basic learning theory: implications for research and practice. *J Neurother*. 2011;15(4):292-304.
74. Cortese S, Ferrin M, Brandeis D, et al. Neurofeedback for attention-deficit/hyperactivity disorder: meta-analysis of clinical and neuropsychological outcomes from randomized controlled trials. *J Am Acad Child Adolesc Psychiatry*. 2016;55(6):444-455.
75. Arnold G, Arns M, Conners K, et al.; the Collaborative Neurofeedback Group. A proposed multisite double-blind randomized clinical trial of neurofeedback for ADHD: need, rationale, and strategy. *J Atten Disord*. 2013;17(5):420-436.
76. Sterman MB, Macdonald LR, Stone RK. Biofeedback training of the sensorimotor electroencephalogram rhythm in man: effects on epilepsy. *Epilepsia*. 1974;15(3):395-416.
77. Lubar JF, Bahler WW. Behavioral management of epileptic seizures following EEG biofeedback training of the sensorimotor rhythm. *Biofeedback Self Regul*. 1976;1(1):77-104.
78. Kotchoubey B, Schneider D, Schleichert H, et al. Self-regulation of slow cortical potentials in epilepsy: a retrial with analysis of influencing factors. *Epilepsy Res*. 1996;25(3):269-276.
79. Kotchoubey B, Strehl U, Holzapfel S, et al. Control of cortical excitability in epilepsy. *Adv Neurol*. 1999;81:281-290.
80. Kotchoubey B, Strehl U, Uhlmann C, et al. Modification of slow cortical potentials in patients with refractory epilepsy: a controlled outcome study. *Epilepsia*. 2001;42(3):406-416.
81. Nagai Y. Biofeedback treatment for epilepsy. [Article in Japanese]. *Nihon Rinsho*. 2014;72(5):887-893.
82. Strehl U, Birkle SM, Wörz S, Kotchoubey B. Sustained reduction of seizures in patients with intractable epilepsy after self-regulation training of slow cortical potentials - 10 years after. *Front Hum Neurosci*. 2014;8:604.
83. Koprivova J, Congedo M, Raszka M, Prasko J, Brunovsky M, Horacek J. Prediction of treatment response and the effect of independent component neurofeedback in obsessive-compulsive disorder: a randomized, sham-controlled, double-blind study. *Neuropsychobiology*. 2013;67(4):210-223.
84. Choi SW, Chi SE, Chung SY, Kim JW, Ahn CY, Kim HT. Is alpha wave neurofeedback effective with randomized clinical trials in depression? A pilot study. *Neuropsychobiology*. 2011;63(1):43-51.
85. Faraone SV, Buitelaar J. Comparing the efficacy of stimulants for ADHD in children and adolescents using meta-analysis. *Eur Child Adolesc Psychiatry.* 2010;19(4):353-364.
86. Molina BS, Hinshaw SP, Swanson JM, et al.; MTA Cooperative Group. The MTA at 8 years: prospective follow-up of children treated for combined-type ADHD in a multisite study. *J Am Acad Child Adolesc Psychiatry*. 2009;48(5):484-500.
87. Riddle MA, Yershova K, Lazzaretto D, et al. The Preschool Attention-Deficit/Hyperactivity Disorder Treatment Study (PATS) 6-year follow-up. *J Am Acad Child Adolesc Psychiatry*. 2013;52(3):264-278.e2.
88. Wang GJ, Boraud T, Volkow ND, et al. Long-term stimulant treatment affects brain dopamine transporter level in patients with attention deficit hyperactive disorder. *PLoS ONE*. 2013;8(5):e63023.
89. Arnold VK, Feifel D, Earl CQ, Yang R, Adler LA. A 9-week, randomized, double-blind, placebo-controlled, parallel-group, dose-finding study to evaluate the efficacy and safety of modafinil as treatment for adults with ADHD. *J Atten Disord*. 2014;18(2):133-144.
90. DeBeus R, Kaiser D. Neurofeedback with children with attention deficit hyperactivity disorder: a randomized double-blind placebo-controlled study. In: Coben R, Evans J, eds. *Neurofeedback and Neuromodulation: Techniques and Applications*. San Diego, CA: Elsevier; 2011:127-152.