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Review

Clinical efficacy and potential mechanisms of neurofeedback

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ABSTRACT

Although many psychological disorders have significant basis in neurobiological dysfunction, most treatment approaches either neglect biological aspects of the problem, or approach dysfunction through pharmacological treatment alone, which may expose individuals to negative side effects. In recent decades, neurofeedback has been promoted as an alternative approach to treating neurobiological dysfunction. Neurofeedback helps individuals gain control over subtle brain activity fluctuations through real-time rewards for pre-established target brainwave frequencies at specific cortical locations. This paper reviews the effectiveness of neurofeedback in a range of conditions, including ADHD, autism spectrum disorders, substance use, PTSD, and learning difficulties. Neurofeedback has emerged as superior or equivalent to either alternative or no treatment in many of the examined studies, suggesting it produces some effects worthy of further examination. In light of its potential to address neurobiological dysfunction directly, future research is suggested in order to refine protocols, as well as to establish effectiveness and efficacy. Potential mechanisms of neurofeedback are discussed, including global connectivity, neuroplasticity, and reinforcement of the default mode network, central executive network, and salience network.

1. Introduction

Clinicians and researchers have long searched for ways to influence minds toward optimal functioning. However, many methods for influencing brain activity, such as surgery, psychopharmacology or electroconvulsive therapy, are invasive or produce profound side effects. Talk therapy is often effective, but some conditions require an integrated biological and cognitive approach. Neurofeedback is an alternative approach that aims to help individuals alter brain activation without introducing electrical or magnetic activity, or pharmacological compounds into the brain, hence preventing the brain from becoming dependent on outside influences for better functioning. However, while this approach may be conceptually appealing, there have been few rigorous studies to establish its efficacy and effectiveness. This review summarizes different neurofeedback protocols and details efficacy findings in a wide range of conditions. Potential mechanisms of change and directions for future research and clinical practice are also discussed.

1.1. Biofeedback

Biofeedback allows individuals to gain control over their physiology by providing real-time reflection of biological activity. Biofeedback has been demonstrated as an effective treatment for conditions such as hypertension, incontinence, headaches, and others (see Association for Applied Psychophysiology, 2008 for an extensive review). Neurofeedback involves measures of brain activity, such as Electroencephalography (EEG) or real time functional magnetic resonance imaging (RTfMRI). Less expensive, safer, and simpler to administer, EEG neurofeedback has been studied more extensively than RTfMRI and is the focus of this review.

1.2. EEG neurofeedback protocols

EEG measures scalp wave frequencies classified as delta (1–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), beta (13–30 Hz), gamma (30–100+ Hz,) and 12–15 Hz representing sensorimotor rhythm (SMR). These protocols utilize the International 10–20 System of placement (Jasper, 1958). Below, different neurofeedback protocols are summarized:

1.3. Beta/SMR

Beta waves represent alertness and active concentration (Haenschel, Baldeweg, Croft, Whittington, & Gruzelier, 2000), while SMR is associated with semantic processing and sustained attention (Egner & Gruzelier, 2001). SMR neurofeedback training appears to strengthen thalamic inhibitory function (Sterman, 1996), and has been applied to learning disabilities or attention deficit and hyperactivity disorder (ADHD), as well as to seizure disorders. Some protocols that aim to increase attention combine upregulation of Beta/SMR with downregulation of theta, which is referred to as theta/beta.

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1.4. Alpha/theta

These frequencies are targeted for upregulation in disorders of hyperarousal such as posttraumatic stress disorder (PTSD). Beyond therapeutic benefits, alpha/theta training may enhance creativity. High-level musicians and dancers trained with this protocol performed better under stressful conditions (Egner & Gruzelier, 2003; Raymond, Sajid, Parkinson, & Gruzelier, 2005).

1.5. Slow cortical potential (SCP) training

SCPs are short (hundreds of milliseconds), event-related brain responses. Positive SCPs represent behavioral inhibition for the purpose of attention (Birbaumer, Elbert, Canavan, & Rockstroh, 1990). The contingent negative variation (CNV) represents event anticipation, and is inhibited in some attention disorders (Banaschewski & Brandeis, 2007). Upregulating CNV was found to improve attention (Gevensleben et al., 2009a, 2009b).

1.6. Alpha asymmetry

Relatively higher right over left prefrontal activity relates to internalizing (depressive, anxious) symptoms (Davidson, 1998). Alpha Asymmetry protocol, or ALAY, aims to reduce left alpha activity (with alpha activity representing neural hypoactivity) and increase right frontal alpha activity, in aim of reducing susceptibility toward negative emotions (Baehr, Rosenfeld, & Baehr, 1997).

1.7. qEEG

Quantitative EEG (qEEG) is a whole-brain mapping approach. Some qEEG approaches attempt to bring individuals closer to a healthy qEEG norm (Thornton, 2000). Other approaches use qEEG to identify hypoactive or hyperactive target regions for training (Logemann, Lansbergen, Van Os, Böcker, & Kenemans, 2010).

1.8. Infralow frequency

A newer approach, infralow frequency neurofeedback targets frequencies as low as 0.01 Hz (Legarda, McMahon, & Othmer, 2011). Few studies have been published using this technique, though some evidence suggests it is a future direction for PTSD or other disorders (Legarda et al., 2011; Othmer, Othmer, & Legarda, 2011).

1.9. RTfMRI

fMRI measures blood flow through blood-oxygen level dependence signal (Ogawa, Lee, Kay, & Tank, 1990). fMRI shows better spatial resolution than EEG, but transformations required for signal processing mean that feedback is currently provided at a 3–5 s delay (deCharms et al., 2005). This approach is developing and has been applied to conditions such as pain and tinnitus.

Below, findings from a broad range of neurofeedback studies are summarized and future directions for research are discussed. To investigate this literature, a systematic search was undertaken using the PubMed/Medline (http://www.ncbi.nlm.nih.gov/sites/entrez) and PsycInfo (http://www.apa.org/pubs/databases/psycinfo/index.aspx) databases. The following search terms were used: "neurofeedback" or "EEG biofeedback;" "controlled," "control group," "RCT" or "randomized." Articles were restricted to those written in English and using human subjects. References of selected articles were also examined. Articles were discarded for small groups or unclear methods. Publications between 1st of January 1960 and 31st of July 2012 were examined.

Table 1 summarizes RCT study findings, organized by target condition. The table provides effect sizes (ES) when available or calculable. If several measures were reported, ES were averaged. ES reported in the paper or in correspondence with authors are bolded and specified as between or within group. Calculated ES were done so using the program *dstat* (Johnson, 1989), using within group results from reported χ^2 values, within-group pre-post *F*-test values, or pre-post means and pooled standard deviations. Starred values indicate significant interactions, i.e. findings that neurofeedback produced superior effects to control conditions using analysis of variance. When available, follow-up ES are reported.

Most studies excluded participants who were comorbid for any other condition or who exhibited organic brain disorders. This review focuses on studies that use rigorous methodology, with randomized clinical trials (RCT) design. Table 1 includes sample description, ES and design characteristics for these studies.

2. Review of neurofeedback literature

2.1. ADHD

At least seven RCT studies exist for ADHD neurofeedback, several with follow-up articles. The first found a significant average increase of 9.3 IQ points (Cohen's $d = 0.76$) in a theta/beta experimental group, as well as significant reductions in inattentive behavior ($d = 0.69$; Table 1: Linden, Habib, & Radojevic, 1996). Theta/beta or SMR training was replicated in several additional RCTs (Table 1: Lévesque, Beauregard, & Mensour, 2006; Steiner, Sheldrick, Gotthelf, & Perrin, 2012). Like theta/beta, SCP training was also found to produce positive changes in ADHD symptomatology, suggesting that both methods enhance regularity mechanisms and produce similar global results in the brain (Table 1: Gevensleben et al., 2009a, 2009b; Wangler et al., 2011). In contrast, one matched control study found SCP training to be more effective ($d = 0.92$) than theta/beta ($d = 0.35$; Leins et al., 2007). Follow-up studies have suggested that effects of both approaches endure, with ds = 0.71 and 0.78 reported for ADHD symptoms at 6 months (Gevensleben et al., 2010; Leins et al., 2007).

Enduring brain activity changes were found, both in amplitude of SCP response differences between activation and deactivation tasks, and in decreased theta/beta ratios (Leins et al., 2007) after the respective forms of training. fMRI found that theta/beta + SMR training in children increased activity in the left caudate nucleus and right anterior cingulate cortex (ACC), regions involved in selective attention, learning and memory (Lévesque et al., 2006). These regions are anatomically distant from the Cz training cite, suggesting neurofeedback acts through neural connectivity. A double-blind procedure was implemented in a small RCT of 14 children, which targeted SMR at points determined by qEEG assessment (Table 1: Lansbergen, van Dongen-Boomsma, Buitelaar, & Slaats-Willemse, 2011). This study found no significant improvements after neurofeedback, and the authors suggested that the double-blind procedure was less effective than manually adjusted single-blind procedures, though this has yet to be replicated.

In summary, neurofeedback has been found to be effective in the treatment of ADHD in several controlled studies, with ES ranging from 0.35 to 1.15, but was also found ineffective in at least one investigation. Protocols typically involve upregulation of SMR or beta frequencies and downregulation of theta frequencies, or modification of SCP responses. Four studies found comparable effects to assisted attention skills training, a proven approach, qualifying

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Table 1
RCT studies of the effects of neurofeedback intervention.

Author (year)	*N* (experimental vs. control), percentage male; age	Target condition	Neurofeedback approach; electrode placement; number of sessions	Control group	Outcome measures	ES (Cohen's d)	Follow up ES (months post treatment)
Linden et al. (1996)	9,9; Not reported; 5–15 yr	ADHD	Theta/beta; Cz Pz; 40	Waiting control	Inattention, IQ	0.73	–
Lévesque et al. (2006)	15,5; 80% male; 10.2 yr	ADHD	Theta/beta + SMR; Cz; 40	Waiting control	ADHD symptoms	0.54*	–
Gevensleben et al. (2009a)	51,26; 82% male; mean: 9.6 yr	ADHD	Theta/beta, SCP; Cz; 36	Attention skills computerized training	ADHD symptoms	**WG: 0.60**	–
Gevensleben et al. (2009b)	46,26; 85% male; mean 9.2 yr	ADHD	Theta/beta, SCP; Cz; 35	Attention skills computerized training	ADHD symptoms	**BG: 0.67**	**BG: 0.71**
Wangler et al. (2011)	59,35; 80% male; mean; 9.4 yr	ADHD	Theta/beta, SCP; CNV Cz, P300 at Pz; theta beta at cz; 40–50	Attention skills computerized training	Continuous performance task (CPT)	**BW: 1.15**	–
Lansbergen et al. (2011)	8,6; 93% male; mean: 10.2 yr	ADHD	SMR; Based on qEEG; 30	Double-blind, sham feedback	Inattention, impulsivity, clinical global impression	–	–
Steiner et al. (2012)	52% male; mean 12.4 yr	ADHD	Theta/beta; Based on qEEG; 40	Attention skills computerized training	ADHD symptoms	**WG: 0.43**	
Kouijzer et al. (2010)	10,10; 15% male; 8–12 yr	Autism; ASD	Reducing theta power; Cz Fz; 40	Waiting control	Social behavior	1.45*	0.87* (6)
Pineda et al. (2008)	Study 1: 4,3 study 2: 9,10; 84% male; mean: 9.8 yr	Autism	Study 1: mu 8–13, study 2: high mu 10–13	Randomized sham feedback	Autistic symptoms, cognitive performance, attention	–	–
Breteler et al. (2010)	10,9; 58% male; mean:10.3 yr	Dyslexia	Normalization to qEEG atlas; Based on qEEG; 20	Treatment as usual (TAU) language training	Spelling	**WG: 0.26**	–
Cho et al. (2004)	3 Groups: 9,10,9; 100% male; 14–18 yr	Social and learning difficulties	Beta/SMR; Cz; 8	Virtual Reality NF, NF, waiting control	CPT	–	–
Peniston and Kulkosky (1989, 1990)	10,10; 100% male; mean: 45.1 yr	Substance use (alcohol)	Alpha/theta; o1; 30	TAU substance use therapy	Relapse	–	2.12* (13)
Scott et al. (2005)	60,61; 60% male; mean: 32.4 yr	Substance use	Beta/SMR, then alpha/theta; C3-FPz for beta, C4-Pz SMR, Pz alpha/theta; 30	Therapy	Abstinence at one year	–	0.47* (12)
Peniston and Kulkosky (1991)	15,14; 100% male; mean: 36.1 yr	PTSD	Alpha/theta; o1; 30	TAU	Depression	–	1.30* (30)
Choi et al. (2011)	12,11; 23% male; mean: 28.6 yr	Depression	Decrease left alpha (increase left activity); F3 F4 Cz; 10	Psychotherapy - assessment, feedback, psychoeducation	Depression	1.06*	–
Cortoos et al. (2010)	9,8,12; 65% male; Mean: 41.5 yr	Insomnia	Teleneurofeedback - Increase SMR, suppress theta + beta; Fpz Cz: 20+	Tele-EMG biofeedback (8); waiting control (12)	Total sleep time	1.04*	–
Hoedlmoser et al. (2008)	16,11; 48% male; mean: 23.6 yr	Nonclinical population sleep study	SMR; C3; 10	Randomized frequency conditioning protocol	Memory, sleep onset and spindle frequency	**WG: 0.7**	–
Kayiran et al. (2010)	18,18; 0% male; mean: 32.1 yr	Fibromyalgia	SMR; C4; 20	Escitalopram	Pain measures, depression, anxiety	–	–
Becerra et al. (2012)	7,7; 36% male; mean 66.6 yr	Nonclinical population at risk for cognitive disorder	Reduce Theta; Based on qEEG; 30	Randomized sham feedback	IQ	–	
Logemann et al. (2010)	14,13; 11% male; Mean: 21.0 yr	Nonclinical population with high impulsivity scores	Beta/SMR; Based on qEEG; 30	Randomized sham feedback	Self report-impulsivity	0.06	–

(*continued on next page*)

Table 1 (*continued*)

Author (year)	*N* (experimental vs. control), percentage male; age	Target condition	Neurofeedback approach; electrode placement; number of sessions	Control group	Outcome measures	ES (Cohen's d)	Follow up ES (months post treatment)
Egner and Gruzelier (2003)	8,9,9,35; 30% male; mean: 23.1 yr	Nonclinical high level musicians	Group 1: alpha/theta; group 2: beta1; group 3: SMR; C3 for beta1; C4 for SMR; Pz for alpha/theta; 10	Alexander technique (n = 10), physical training (n = 16), mental training (n = 9)	Musical performance, anxiety	Alpha/theta Musical performance (0.55); Beta1 anxiety reduction (.96)	–
Ros et al. (2009)	10,10,8; 45% male; mean: 33.5 yr	Nonclinical ophthalmic micro-surgeons	SMR (N = 10); alpha/theta(N = 10); Cz for SMR, Pz for alpha/theta; 8	Waiting control	Surgical technique, surgical skill	**WG: 0.56**	–

Notes: RCT = randomized control trial; SMR = sensorimotor rhythm (12–15 Hz); BG = between group; WG = within group; starred (*) ES show significant interaction, i.e. time *x* condition interaction shows neurofeedback superior to control group; bolded ES indicated ES reported in the publication.

neurofeedback for ADHD as efficacious and specific by the guidelines of Chambless et al. (1998). It would be beneficial to compare neurofeedback to established stimulant medication in future research, in addition.

2.2. Autism and autistic spectrum disorder

Autistic spectrum disorders (ASD) are characterized by excessive and disorganized connectivity within the frontal lobe (Courchesne & Pierce, 2005), unusual lateralization (Dawson, Warrenburg, & Fuller, 1982) and excessive coherence, representing brain hyperconnectivity (Cantor, Thatcher, Hrybyk, & Kaye, 1986). The first small matched-control study of neurofeedback for autism relied on heavy adjustments to a μ (10–13 Hz) enhancing frequency protocol depending on the child's specific symptoms (Jarusiewicz, 2002). Over an average of 36 sessions, neurofeedback improved autistic behavior by 26% in the experimental group.

Another matched-control study used both qEEG and infrared imaging to assess connectivity in the brain before creating protocols (Coben & Padolsky, 2007). Training was aimed at reducing hyperconnectivity, typically in posterior-frontal to anterior-temporal regions. Neurofeedback participants showed significant improvements (40%) in ASD symptomatology (d = 1.12). Hyperconnectivity was "decreased or showed no change" in 77% of participants.

Using a matched-control group versus experimental group of 7 children each (12 boys, 2 girls, mean age 10.1 years), theta/SMR training significantly improved social functioning (d = 0.62) and communication (d = 0.73) in children with ASD, though not for all children. Significant changes in pre and post qEEG assessment suggested that the brain activity changes endured past training. Improvements were observed in auditory attention, impulse inhibition, set shifting, concept generation and goal setting, but not processing speed, visual attention, or verbal and geometric memory. Specific ES were not provided, but a 12 month follow-up of this study found maintenance of improvements in social behavior and executive function (Kouijzer, de Moor, Gerrits, Buitelaar, & van Schie, 2009a).

Random assignment to mu-reward training as opposed to sham-EMG training found that neurofeedback significantly reduced coherence between cross-hemispheric sites, reduced mu, increased attention, and significantly improved autistic spectrum behavior (Table 1: Pineda et al., 2008). However, in this study, parent rating of sensory/cognitive awareness worsened, suggesting that neurofeedback may improve certain symptoms while worsening others. This is a significant concern, and must be addressed in future research.

Based on Kouijzer, de Moor, Gerrits, Congedo, & van Schie, 2009b, an additional RCT focused on reducing theta power. Neurofeedback produced significant improvements in social functioning and set shifting, but not in attention control, concept generation, goal setting or speed/efficiency or other executive function measures (Table 1: Kouijzer, van Schie, de Moor, Gerrits, & Buitelaar, 2010). Significant improvements were also found in social awareness (but not other realms of social interaction) and in social communication. Neurofeedback did not produce significant effects in stereotyped behavior, or most communication measures from the children's communication checklist (CCC-2; Bishop, 2003). The improvements that were found endured 6 months post-treatment (Kouijzer et al., 2010).

In summary, neurofeedback approaches for autism often use mu (10–13 Hz) or SMR training. Results of these studies have been mixed, with some finding improvements in autistic behavior, neuropsychological measures, and cognitive function (ES 1.12 and 1.45) but others finding that specific functions improve while other functions do not, or even symptom worsening.

2.3. Intellectual and learning disabilities

In a match-controlled study, 10 children with learning disabilities were assigned to reduce theta/alpha ratio, or to sham randomized feedback. Results suggested that neurofeedback improved attention (measured by a continuous performance task; CPT) as well as verbal and performance IQ (Fernández et al., 2003). At a two-year follow-up, the experimental group's attention gains endured, as well as their performance IQ, but the verbal IQ scores dropped in both experimental and control group children (Becerra et al., 2006). A replication study found improvements over controls in the CPT test for reaction times, omission errors, and commission errors. Small but significant gains were also observed in IQ score in the experimental but not in the control group (Fernández et al., 2007). In an uncontrolled study, 23 intellectually disabled patients (ranging from mild to moderate disability) showed increases in IQ performance, CPT performance, and decreases in behavior problems after 80–160 sessions of qEEG based neurofeedback training (Surmeli & Ertem, 2010).

In a group of undiagnosed individuals with social and learning difficulties, neurofeedback Beta training was applied with or without a virtual reality immersive environment (Table 1: Cho et al., 2004). This RCT found gains in CPT performance following neurofeedback, which were enhanced in the virtual reality condition. Another RCT used qEEG guidance to reduce slow wave activity or decrease coherence in dyslexic patients. While this approach may be closer to what a patient may experience in working with a clinician, improvements were not observed for any measure except spelling, where gains were small ($d = 0.26$; Table 1: Breteler, Arns, Peters, Giepmans, & Verhoeven, 2010).

To date, no controlled study of learning disabilities has found large ES for improvements in cognitive functioning or IQ. Several studies found small gains in IQ and spelling, and gains in CPT performance.

2.4. Epilepsy

Neurofeedback as a treatment for epilepsy first emerged in findings that 12–15 Hz training protected cats against monomethylhydrazine-induced seizures (Sterman, Fairchild, & Van Twyver, 1968). One ABA design study found that 12–15 Hz upregulation normalized EEG patterns during sleep, which was presented as evidence against placebo effect (Whitsett, Lubar, Holder, Pamplin, & Shabsin, 1982). Significant reductions in seizures were found following 35 SCP training sessions from 3.3 to 2.2 average seizures weekly ($d = 0.36$; Kotchoubey et al., 2001). These results suggest that neurofeedback is unlikely to replace medication for seizure disorders, but could be used in combination, a prospect for future research. Notably, this study used SCP as the neurofeedback training approach, whereas past uncontrolled research has focused on 12–15 Hz training, obtaining ES between $d = 0.2$–1.4, and mostly within the range of medium to large (Tan et al., 2009).

2.5. Substance use

Early work with alpha/theta protocols on individuals with alcohol dependence found decreased drinking behavior and depression, as well as widespread personality changes, which persisted at a 4 year follow-up (Table 1: Peniston & Kulkosky, 1989, 1990). Participants were also found to have significantly lower risk of relapse at a 13 month follow-up than the control group.

A more recent RCT study of 121 participants with substance abuse disorders employed both beta/SMR and alpha/theta neurofeedback (Table 1: Scott, Kaiser, Othmer, & Sideroff, 2005). A wide range of outcomes were measured, including days in treatment, sobriety, attention, and personality using the Minnesota Multiphasic Personality Inventory-2 (MMPI-2; Butcher et al., 2001). Forty-six percent of treatment as usual (TAU) subjects dropped out of the study, while only 24% of neurofeedback subjects did. Using the neurofeedback protocol, participants remained in treatment 37 days longer, were sober in 77% percent of cases at the one year follow-up (compared with 44% of TAU; $d = 0.47$). Experimental but not control subjects exhibited significant MMPI-2 scale reductions in depression, hypochondriasis, hysteria, schizophrenic, and social introversion scales. Effects of the training did not differ across different drugs of choice. Similar to the findings of Peniston and Kulkosky, widespread MMPI-2 changes suggest some global changes as the result of training.

In summary, two protocols have been applied to substance use disorders: an alpha/theta protocol, and a modified alpha/theta protocol with SMR/beta-training sessions. These studies found reductions in addiction behavior, and positive personality shifts as measured by validated instruments.

2.6. PTSD

Peniston and Kulkosky (1991) (Table 1) used their alpha/theta protocol with a sample of veterans with PTSD. Every participant in the experimental group had reduced psychoactive medication consumption by the end of the treatment, while only one of the control participants had done the same. Using the MMPI, both groups showed decreases on the schizophrenia scale, but only the experimental group showed reductions in hypochondriasis, depression, hysteria, psychopathic deviation, paranoia, psychasthenia, hypomania, introversion, and the PTSD subscales. At a 30 month follow-up, all 14 participants in the TAU group and only 3 out of 15 experimental participants relapsed.

At the 2011 conference of the Naval Center's Combat & Operational Stress Control (COSC), infralow data collected at Marine Corps Base Camp Pendleton were presented. Data was collected from over 350 active duty service members experiencing combat-related symptoms, many of whom showed remission of numerous symptoms following neurofeedback training of frequencies as low as 0.01 Hz (Villanueva, Benson, & LaDou, 2011). This study tracked up to 45 concurrent symptoms, such as flashbacks, nightmares, migraines, irritability, lack of motivation, poor sleep quality, depression, and others. In conjunction with alpha/theta training, participants received approximately 20 infralow neurofeedback sessions in targets based on patient symptoms and response.

Although it was not controlled research, large ES were reported by the Navy for specific symptoms associated with PTSD, such as 0.84 for depression, 0.8 for sleep related symptoms, 0.96 for motivation improvement, and 0.5 for migraines. The authors of the study argue that in witnessing improvement in such disparate symptoms, they provide evidence that infralow neurofeedback strengthens widespread regulatory networks (Villanueva et al., 2011). This study is undergoing institutional review board approval, and further RCT research is being planned to investigate this potential treatment more systematically (personal communication with Dr. Anna Benson, clinical psychologist and principal investigator at Naval Hospital Camp Pendleton).

2.7. Depression

One neurofeedback method for depression involves reversing right frontal asymmetry (Baehr, Rosenfeld, & Baehr, 2001; Baehr et al., 1997), which is associated with internalizing (depressive, anxious) symptoms (Davidson, 1998). In the alpha asymmetry (ALAY) approach, individuals learn to decrease the ratio of right over left frontal activity. The first RCT ALAY study was published

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in 2010 (Table 1: Choi et al., 2011). In 10 sessions, this study observed clinically significant changes in depression ($d = 1.06$), and average depression symptoms fell significantly more than a "placebo psychotherapy" group that underwent assessment and psychoeducation. Alpha/theta and infralow neurofeedback were found to produce relief from depression in other studies, and may be a worthwhile avenue for future research.

2.8. Sleep

SMR upregulation had been linked to sleep enhancement in early research (Sterman, Howe, & Macdonald, 1970). In the first RCT study of teleneurofeedback (performed at home through internet connection and the clinician on the telephone), SMR upregulation significantly increased sleep time ($d = 1.04$) and reduced time spent awake after sleep onset over both EMG biofeedback and waiting control (Table 1: Cortoos, De Valck, Arns, Breteler, & Cluydts, 2010). An RCT design study with nonclinical participants found that SMR upregulation significantly enhanced sleep onset latency ($d = 0.7$) and spindle frequency (Table 1: Hoedlmoser et al., 2008). Lastly, COSC data found an ES of 0.8 for sleep symptom improvement in their subjects, and so infralow frequency neurofeedback may be a future research direction (Villanueva et al., 2011).

2.9. Pain

In a rater-blind RCT, female fibromyalgia patients were assigned to SMR-training or to an escitalopram control group. Neurofeedback produced significant reductions of moderate to large ES above escitalopram for pain, fatigue, anxiety and depression (Table 1: Kayiran, Dursun, Dursun, Ermutlu, & Karamürsel, 2010). One study of children with migraines found significant reductions in number of migraines experiences post SCP training (Siniatchkin et al., 2000), but this has not yet been studied in a controlled manner.

2.10. Nonclinical populations

Neurofeedback has been found to improve mental rotation (Hanslmayr, Sauseng, Doppelmayr, Schabus, & Klimesch, 2005), continuous performance (Egner & Gruzelier, 2004), and attention (Egner & Gruzelier, 2001), but few randomized trials have been performed. One attempt to reduce impulsivity with beta/SMR upregulation found that neurofeedback was not more successful than sham control (Table 1: Logemann et al., 2010). In healthy elderly participants, an RCT found small but significant IQ increases after theta reduction training, and no difference between control (sham feedback) and experimental groups in attention or memory (Becerra et al., 2012). This study found that absolute EEG power changed only in the experimental group after training, but relative power shifted in both groups, raising questions of placebo effect.

In ophthalmic surgeons randomly assigned to SMR-training, alpha/theta training, or waiting-control, SMR-training significantly improved surgical skills as assessed by a suturing task ($d = 0.87$) and by evaluation of superiors ($d = 0.62$; Table 1: Ros et al., 2009). This study used only 8 sessions of training, considered a small number.

A pilot study performed at the Royal College of Music in London randomly assigned 61 high level musicians to SMR-training, alpha/theta training, beta1 (15–18 Hz) training, Alexander technique, physical exercise, or mental exercise (Table 1: Egner & Gruzelier, 2003). Although participants underwent only ten 15 min sessions of training, alpha/theta training emerged as beneficial to musical performance enhancement as measured by musicality, stylistic accuracy, interpretative imagination, and overall quality ($d = 0.55$), over SMR neurofeedback. None of the non-neurofeedback participants showed significant improvements in musical performance post training.

Training alpha power has also been linked with cognitive and performance enhancement (Hanslmayr et al., 2005). Upregulating peak alpha performance improved mental rotation in 14 healthy participants (Zoefel, Huster, & Herrmann, 2011), as well as executive function and processing speed, but not memory in six healthy participants of ages 70–78 years (Angelakis et al., 2007). Archers, randomly assigned to left hemisphere alpha training performed better than those assigned to right hemisphere alpha training or waiting control (Landers et al., 1991). Similarly, both alpha/theta neurofeedback and heart rate variability biofeedback produced better technique, timing, and performance flair over waiting control in a group of dancers (Raymond et al., 2005).

In summary, neurofeedback appears to produce some performance and cognitive enhancement, with theta/beta/SMR showing more cognitive enhancement and alpha/theta more creativity enhancement. Alpha and theta waves are known to be predominant in meditation states (Cahn & Polich, 2006), and so it is possible that these forms of neurofeedback may produce similar positive effects on attention and focus as meditation (Chan & Woollacott, 2007).

2.11. RTfMRI

RTfMRI is relatively nascent (Cox, Jesmanowicz, & Hyde, 1995), and findings are preliminary. One condition for which RTfMRI shows potential is pain. In three 13 min sessions, randomly assigned healthy participants learned to exert control over their rostral anterior cingulate cortex (rACC), which helped them control pain response to a painful condition in a post-training scan that took place later in the day (deCharms et al., 2005). Eight chronic pain patients underwent the same training procedure, and reported reduced pain levels over a control group ($N = 4$) that received autonomic biofeedback (deCharms et al., 2005). No follow-up data were produced, and it remains unclear to what extent such minimal training would endure over time. One follow-up study of tinnitus did find some minimal enduring effects two weeks post training aimed to reduce auditory cortex activation over 4 sessions of 4.5 min; minor symptom reduction was observed in 2 out of 6 patients (Haller, Birbaumer, & Veit, 2010). Replication of these results is warranted.

RTfMRI has also been applied to mood. In a single day, nine healthy volunteers underwent four 4 min training sessions, which focused on activating the anterior insulate cortex, an area involved in emotional regulation (Caria et al., 2007). Later in the day, participants were able to activate and deactivate their insula. Eight participants learned to decrease sACC activity, associated with mood disorders (Critchley, 2005), but effects did not endure at post-treatment scans later in the day (Hamilton et al., 2011). RTfMRI work is relatively recent, but therapeutic utility has not yet been demonstrated. Rigorously designed clinical studies may help elucidate the efficacy of RTfMRI.

3. Summary

At least 22 well-controlled neurofeedback studies have been published, with several additional pilot or older studies providing further directions for future research. Figure 1 summarizes ES findings from this review when available.

"Neurofeedback" refers to a broad category of therapies, and different target frequencies have been found to produce different outcomes. For example, SMR training enhanced healthy participants' attention and reduced CPT errors, while beta training reduced reaction times and enhanced arousal (Egner & Gruzelier,

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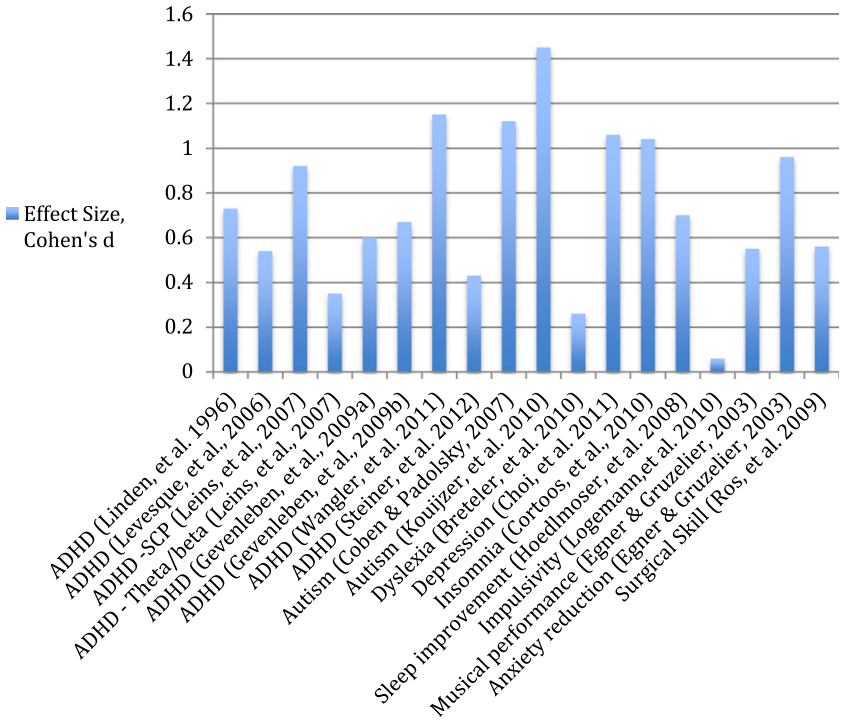

Fig. 1. This figure presents available ES (Cohen's *d*) from the studies examined in this review, organized by condition treated.

2004). Some argue that these findings suggest neurofeedback effects are specific, and not merely placebo. Additionally, different frequencies are reported as easier or harder to selectively train; after eight sessions, SMR amplitudes showed change, whereas theta bands did not (Vernon et al., 2003). Different approaches are often combined in a course of treatments, for example enhancing beta while reducing theta frequencies. Further research is necessary to determine whether ideal protocols exist.

4. Field limitations and future directions

Several limitations arise in reviewing this literature. First, relatively few neurofeedback studies are well-designed, controlled studies, and those that exist are rarely manualized. Because the framework of Chambless et al. (1998) requires manualized protocols and comparisons to established treatments, neurofeedback is only eligible as efficacious and specific for ADHD treatment with theta/beta or SCP. In addition, publication bias means published data is skewed toward the significant and positive. Although the studies reviewed in this paper provide optimistic starting points, considerably more research is necessary to resoundingly demonstrate efficacy and effectiveness. Several studies have implemented double-blindedness successfully, suggesting the approach should be explored further (Arnold et al., 2012; Lansbergen et al., 2011). qEEG or connectivity analysis methods should also be applied, in order to demonstrate measurable differences pre and post treatment that would rule out placebo effects.

In addition to demonstrating efficacy, in order to demonstrate effectiveness and generalizability, neurofeedback must be replicated in diverse populations, considering culture, ethnicity, socioeconomics, and other influences. Additionally, because neurofeedback has been applied to conditions that are often found to be comorbid, future literature should address whether different forms of neurofeedback are equally effective for conditions when they are comorbid, and whether certain protocols may be counter-indicated for certain comorbid conditions.

Of the well-designed studies that exist, only some have investigated pre and post EEG patterns to verify whether neurofeedback produces visible changes in brain activity. Because different protocols target different brain activity frequencies and different locations, studies' results are difficult to pool. For example, it may be that alpha/theta neurofeedback is particularly useful for trauma, but that SMR neurofeedback is not particularly useful for epilepsy, and pooling such studies may hinder the ability to discern these differences.

A controversial problem that arises is that individual brains are unique and therefore creating a manualized protocol may in fact be impractical (Brandeis, 2011). One ADHD study found that children benefited from protocol-modification to match their individual neural profiles (Wangler et al., 2011). However, these modifications were decided upon by researchers with extensive neurofeedback experience. setting practitioner-training standards at very high levels (Brandeis, 2011). However, given the uniqueness of brain, a one-size-fits-all protocol may be unrealistic. Some experts support the clinical neurofeedback model, which allows for trial and error or qEEG based decisions (Sokhadze, Cannon, & Trudeau, 2008). This notion falls in line with emerging trends of personalized medicine, which emphasize the importance of individualizing medical treatments to genetic, endocrine, and neurological profiles. This is a problem that needs to be addressed before manuals can be adequately created for future research and clinical practice.

Another question to consider is whether qEEG is an appropriate guidance tool in that it is unclear whether an 'average brain' is a desirable outcome; it may be better to consider each discrepancy from normed qEEG standards separately to determine if it is adaptive or maladaptive. More research can help to personalize neurofeedback protocols, as well as to identify optimal combinations of neurofeedback with pharmacology or talk-therapy. More investigation is also necessary to see whether neurofeedback affects endocrine, cardiovascular, or other bodily functions.

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5. Potential neurofeedback mechanisms

Another current limitation of the neurofeedback literature is the lack of research and consensus as to underlying mechanism. Below is a summary of different theories about mechanism of neurofeedback, as well as concrete suggestions for studies that may help elucidate their validity.

5.1. Neuroplasticity

It is known that circuitry changes and new neurons appear throughout life (Eriksson et al., 1998). Psychological disorders are characterized by widespread alterations from normal circuitry in limbic, frontostriatal and prefrontal regions (Menon, 2011). Experts now consider ailments such as schizophrenia and addiction to be diseases of circuitry rather than neurochemistry (Balu & Coyle, 2011; Koob & Volkow, 2010). Successful treatment of such disorders is accompanied by plastic changes in the brain, for example through transcranial magnetic stimulation (Speer et al., 2009) or deep brain stimulation (Lozano and Snyder, 2008; Lujan, Chaturvedi, & McIntyre, 2008). Neurofeedback may be producing effects by enhancing synaptic strength through repeated firing. This has been observed using EEG methods in Brain Computer Interface (BCI), with which patients with disabilities learn to move robotic limbs or generate computerized speech through EEG signals. In BCI, neuroplasticity is demonstrated, as individuals become more adept at producing focused neural activity over time (Levine et al., 2000). Neurofeedback may be likewise strengthening circuitry. To investigate this, fMRI connectivity analysis pre and post treatment should be compared to gauge connectivity between targeted regions associated with good functioning.

5.2. Global connectivity/comorbidity

Rather than specific regions of dysfunction, scientists increasingly find network dysfunction in conditions ranging from depression to Alzheimer's disease to schizophrenia (Menon, 2011). An additional clue for network involvement is frequent comorbidity, i.e. disorders co-occurring at rates higher than predicted by chance (Clark, Watson, & Reynolds, 1995), suggesting multiple sites of dysfunction. In addition, connectivity studies show that on average there are only three synapses between any two mammalian cortical neurons (Nunez, 1995). This may explain why dysfunction can have consequences for multiple systems.

Network modeling over the last decade suggests the brain works as a small-world model, characterized by high density of local connectivity, connected hierarchically through more modest connectivity. In the cortex, for example, there is dense connectivity within localized anatomical clusters, and centralized but sparser connectivity between clusters (Bassett & Bullmore, 2006; Hilgetag & Kaiser, 2004). These findings motivate the hypothesis that psychopathology may be grounded in the dysfunction of core networks or their functional integration. If this were so, then neurofeedback methods that regulate connectivity within and between networks would be effective in resolving psychopathologies. In support of this hypothesis, several studies have found that neurofeedback relieves a variety of symptoms simultaneously (Leins et al., 2007; Linden et al., 1996; Scott et al., 2005; Peniston & Kulkosky, 1989, 1990; Villanueva et al., 2011). These widespread changes hinting at strengthened regulatory mechanisms raise questions about core network involvement.

5.3. Core neurocognitive networks: Default Mode Network (DMN), Central Executive Network (CEN) and Salience Network (SN)

At least three core neurocognitive networks have been identified in relation to brain self-regulation pertinent to psychopathology: the DMN, CEN, and SN. This 'Triple network model' (Menon, 2011) is hypothesized to be strongly involved in proper functioning.

The DMN activates during intrinsic activity without external stimulus (Raichle et al., 2001). This network involves portions of the medial prefrontal cortex, medial temporal lobe, posterior cingulate cortex, precuneus, and the medial, lateral and inferior parietal cortex, and has been found to activate during daydreaming (Mason et al., 2007), meditation (Brefczynski-Lewis, Lutz, Schaefer, Levinson, & Davidson, 2007), and autobiographical memory retrieval (Buckner, Andrews-Hanna, & Schacter, 2008). DMN abnormalities have been found in Alzheimer's disease (Buckner et al., 2005), schizophrenia (Harrison, Yücel, Pujol, & Pantelis, 2007), autism (Kennedy, Redcay, & Courchesne, 2006), depression (Hamilton et al., 2011), and ADHD (Broyd, Helps, & Sonuga-Barke, 2011), suggesting it may serve a regulatory function in a healthy brain. Long-term practice of meditation strengthens DMN connectivity (Jang et al., 2011), and is known to improve disparate symptoms (Baer, 2003), much like neurofeedback appears to do. Some neurofeedback experts posit that neurofeedback regulates DMN activity, which improves the brain's self-regulation capabilities (Othmer et al., 2011).

The CEN is based in the dorsolateral prefrontal cortex and the lateral posterior parietal cortex (Sridharan, Levitin, & Menon, 2008), and is involved in maintaining and applying memories to cognitive tasks, and other executive functions. Deficits in the CEN have been found in schizophrenia, Alzheimer's disease, autism, depression, and other psychopathological conditions (Menon, 2011). The SN is a system involved in integrating and regulating somatic, autonomic and emotional information. It includes the anterior insula (AI), anterior cingulate cortex (ACC), as well as the subcortical areas of the amygdala and substantia nigra/ventra tegmental area (Seeley et al., 2007). These are areas known to be involved in anxiety, depression, addiction, and impulse control disorders, amongst others (Menon, 2011). Deficits in the SN have also been found in pathology ranging from schizophrenia (Palaniyappan, Mallikarjun, Joseph, White, & Liddle, 2010; White, Joseph, Francis, & Liddle, 2010), to Alzheimer's disease and frontotemporal dementia (Zhou et al., 2010).

The Triple network model of psychopathology posits that dysfunction in any one of these networks affects all three, leading to symptoms that may appear removed from the original dysfunction or diagnosis. In support of this, Menon (2011) cites known deficits of multiple networks in a given condition, for example DMN and SN in pain (Baliki et al., 2008) and depression (Berman et al., 2011), and deficits in all three networks in schizophrenia (Palaniyappan et al., 2010).

Another relevant property of these networks is that they oscillate at slow cortical potential frequencies of 0.01 Hz or below (Fox, Snyder, Zacks, & Raichle, 2005; Fransson, 2005; Menon, 2011; Nir, Hasson, Levy, Yeshurun, & Malach, 2006; Nir et al., 2008; Taylor, Seminowicz, & Davis, 2009). Such infralow frequencies are utilized in newer forms of neurofeedback, such as those employed by the COSC Navy clinicians (Villanueva et al., 2011) and other recent work (Legarda et al., 2011; Othmer et al., 2011), which has produced improvements in a wide range of symptoms. Neurofeedback that targets lower frequencies such as these and alpha/theta may directly affect these networks, thereby producing widespread symptom improvement. This theory could be verified through connectivity analysis with fMRI or diffusion tensor imaging that examines activity in these networks pre and post neurofeedback training.

It is important to note developmental implications of neurofeedback with regard to neuroplasticity and network development. The rapidly developing child or adolescent brain is likely more malleable than the adult brain, and hence neurofeedback may produce stronger, faster, or more permanent effects. This suggestion should

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be directly examined in future research comparing adult and pediatric patients in similar protocols, and if it is supported, several implications are important to consider. For example, this would suggest that neurofeedback has potential to lay groundwork for optimal organization in young minds as these networks develop, and may be used in a preventive manner. On the other hand, it could be argued that if misused, neurofeedback has equal potential to dysregulate adult networks as they form and strengthen. More research into the effects of different forms of neurofeedback on the developing brain is needed, and researchers and clinicians must exert heightened caution in monitoring pediatric patients closely, vigilantly searching to symptoms that suggest protocols may be causing harm rather than good.

6. Conclusions

Neurofeedback alters brain activity intrinsically, without introducing new elements such as electrical activity, magnetic activity, or pharmacological agents, into the brain. It has been found to produce symptom relief and changes in brain activity that endure over time in at least some psychological disorders. The theoretical appeal of neurofeedback over other therapeutic methods is its intrinsic nature, wherein the brain is taught to produce more adaptive activation rather than to depend on external stimuli in order to correct dysfunction. However, the few controlled studies that exist are insufficient to resoundingly declare therapeutic success in all conditions but ADHD. More and better-organized research is necessary to confirm the efficacy and effectiveness of neurofeedback, as well as to fully investigate its mechanism of action and explore personalized medicine or combination therapy approaches. However, the data that exists provides reason for cautious optimism. With further research aimed to optimize and personalize neurofeedback, these methods may enrich current approaches to neurological and psychological dysfunction.

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