Article

The Effectiveness of Neurofeedback Therapy as an Alternative Treatment for Autism Spectrum Disorders in Children

A Systematic Review

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Abstract: Findings for the effectiveness of neurofeedback in autism spectrum disorder are found to be inconsistent. Therefore, this review comprehensively and systematically reviewed literature on the effectiveness of neurofeedback for the treatment of autism spectrum disorders in children. A systematic search of Embase, Medline, Web of Science, PsycINFO, Cochrane, and Google Scholar was carried out in October 2017 to find relevant papers. We selected full journal articles that reported neurofeedback as a treatment for autism in children (0–17 years). The search yielded 587 articles and we included 20 references with a total of 443 participants. Ninety-four percent of nonrandomized controlled and experimental trials concerning neurofeedback for autism spectrum disorders found positive results. The evidence for effectiveness of neurofeedback therapy was even more robust when only randomized controlled studies were considered. Although there are only a few randomized controlled studies, results support effectiveness of neurofeedback for autism spectrum disorder, including long-term positive effects. In the future, optimal treatment protocols have to be developed to guide clinicians in their neurofeedback treatment. In conclusion, neurofeedback seems to be an alternative treatment for autism spectrum disorders, with space for improvement.

Keywords: autism spectrum disorder, electroencephalography, neurofeedback, treatment

Autism spectrum disorder (ASD) is a neurodevelopmental disorder with symptoms that manifest early in the development of the child (American Psychiatric Association, 2013). ASD is also referred to as being a "pervasive developmental disorder." Here, pervasiveness refers to the prevalent and general interference that the disorder has on all domains of the development of the child. Children with ASD are described with having two core symptoms: persistent deficits in social communication and social interaction across multiple contexts, and the presence of restricted, repetitive patterns of behavior, interests and/or activities (American Psychiatric Association, 2013). ASD is no longer considered a rare condition (Baird et al., 2006). Its prevalence during the school years is believed to be slightly higher than 1% of the general population, described as 62 out of 10,000 people having ASD (Elsabbagh et al., 2012; Fombonne, 2009). Furthermore, ASD is more common in boys than girls with a ratio of 4:1 (Fombonne, 2005).

Treatments for Autism Spectrum Disorders

There is evidence that early intensive training programs have lasting beneficial effects on a number of aspects of ASD (Gillberg, 2010), therefore we have chosen to focus our review only on children. The golden standard treatment for autism is therefore (intense) behavioral treatment, or referred to as Applied Behavior Analysis (ABA; Fisher, Piazza, & Roane, 2011; Franken, Muris, & Denys, 2013). ABA refers to a systematical observation and analysis of interactions between behaviors and environment of the

child with ASD. Within ABA therapy, by means of operant conditioning, consequences of observed behavior are adjusted in such a way that desired behavior is increased by an empowering consequence and unwanted behavior is extinguished by an invalidating consequence. ABA therapy is considered to have lasting beneficial effects on a number of aspects of ASD (Voos et al., 2013). Literature points out that increased treatment intensity of behavioral therapy has significant positive effects, but the effect of treatment duration requires further research (Linstead et al., 2017).

Pharmacological therapy is another form of therapy that is often given to children with ASD. However, many of the pharmacological therapies do not treat the core symptoms of ASD (i.e., language and social impairments). Rather, they are often employed in treating the concomitant problematic impairments of ASD (such as hyperactivity, aggression, and mood), thereby allowing for the nonmedical interventions to be more successful (Volkmar, Cook, Pomeroy, Realmuto, & Tanguay, 1999). As an example, medical treatment of ASD with antipsychotics can cause serious side effects such as sedation and dizziness or result in a movement disorder. Therefore it has been advised to evaluate pharmacological treatments on an individual level (Campbell et al., 1997; LeClerc & Easley, 2015).

Most recently, neurofeedback (NF) has been presented as a neurological based therapy in which the neuronal activity is represented with use of auditory stimuli, visual stimuli, or other forms of representation which are subsequently modified to change the oscillation pattern of neuronal activity. Because NF therapy does not cause side effects, interest for this therapy for neurodevelopmental disorders has been growing in recent years (Arnold et al., 2013; Lansbergen, Van Dongen-Boomsma, Buitelaar, & Slaats-Willemse, 2011; Lofthouse, Arnold, Hersch, Hurt, & DeBeus, 2012). Currently, NF has already been shown to produce symptom relief and longitudinal changes in brain activity in attention-deficit hyperactivity disorder (ADHD), another neurodevelopmental disorder (Micoulaud-Franchi et al., 2014; Strehl et al., 2017).

Theoretical Underpinnings of Neurofeedback Therapy

Operant conditioning is considered as the principle learning mechanism underlying the self-regulation of brain activity via neurofeedback therapy. Neurofeedback techniques are commonly based on either electroencephalography (EEG) or real-time functional magnetic resonance imaging (rtfMRI). To our knowledge, there are currently no rtfMRI implementations in ASD. Therefore, our study will only focus on electroencephalographic (EEG) neurofeedback. This is a method that uses EEG technology to provide an individual with information about the electrical activity of the cortex of the brain (Gevensleben, Rothenberger, Moll, & Heinrich, 2012; Willis, Weyandt, Lubiner, & Schubart, 2011). The EEG signals are filtered into frequency bands that are specified in terms of frequency in Hertz (Hz), the number of waves per second. Within NF therapy sensors are placed on the scalp to measure brainwave activity and records of this activity are represented visually or auditory to the patient. When performing a task, the person is rewarded when a brain frequency change occurs in the desired direction. The goal of the therapy is to teach a person how to influence or to control his or her brainwave activity. The four main brain waves that NF therapy focuses on are beta, alpha, theta, and delta waves (Neumann, Strehl, & Birbaumer, 2003). Frequencies lower than 4 Hz are associated with sleep state (delta); 4–7 Hz frequencies (theta) are associated with drowsy, hypnotic, or sleeping states. Alpha waves (8–12 Hz) occur during non-active, wakeful, relaxation states such as rest and meditation. Finally, beta waves are fast 13–30 Hz and are typically present when the brain is highly aroused, mostly during normal waking consciousness or an activity (Zhuang, Zhao, & Tang, 2009).

Objectives

The main goal of this review is to present an overview of studies concerning NF for the treatment of ASD in children. By systematically reviewing the literature concerning neurofeedback for ASD in children, we can answer the question whether NF is an effective alternative treatment in children with ASD.

Methods

This systematic review was designed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Liberati et al., 2009).

Search Strategy

The main goal of this review is to present an overview of studies concerning NF for the treatment of ASD. To answer this question the following bibliographic databases were searched: Embase, Medline, Web of Science, PsycINFO, Cochrane, and Google Scholar. We used a detailed search strategy combining terms associated with neurofeedback, electroencephalography, and autism, which differed slightly between the different databases due to their differences in

thesaurus and structure of the system (the specific syntax strategies are added in the Appendix). The search was created by an experienced medical librarian (W. B.). Two independent reviewers (L. H. and H. F.) screened the titles and abstracts of all papers found in the search to decide if they met the eligibility criteria. Any disagreements were resolved through discussion. No record was kept of these disagreements. The references were stored in the database program EndNote X3 where duplicates were removed. In the EndNote database, further analysis was performed and studies were excluded based on their titles, abstracts, and full text assessment.

Eligibility Criteria

To be selected for this review, the study had to first and foremost report NF as a treatment for ASD in children (< 18 years). The diagnosis for autism had to be diagnosed by DSM-III-R, DSM-IV, or DSM-5 guidelines. Labels of subgroups of ASD (i.e., classic autism, Asperger's, or pervasive developmental disorder not otherwise specified) are recently removed from the newest edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5; American Psychiatric Association, 2013), the standard classification of mental disorders used by mental health professionals. However, studies involving these subgroups were also included in the current review. This reorganization has its pros and cons. In short, DSM-5 provides better specificity (reducing false-positive diagnoses), but at the expense of possibly reduced sensitivity, especially for older patients, individuals without intellectual disability, and individuals who hitherto met criteria for diagnoses of DSM-IV (Lai, Lombardo, Chakrabarti, & Baron-Cohen, 2013). A study had to be published as a full journal article and as so, had to be peer-reviewed. Furthermore, articles were included if they were, for example, a clinical experimental study with within- or between-subject design, with or without a blinded condition, randomized or non-randomized, controlled or non-controlled with a placebo/sham-condition, a waitlist condition or another therapy such as electromyography (EMG) feedback or cognitive behavioral therapy (CBT). Studies that reported follow-up designs or replicated earlier findings were also included. Studies without a control group and without peer review were defined as studies with poor quality (Figure 1). Studies were excluded when they concerned NF for adults or other disorders such as ADHD, learning disorders, intellectual disorders etc. Single case studies or book chapters were not considered because of their narrative character. Finally, no language restrictions were imposed. However, no suitable papers in other languages than English were found.

Data Extraction

Data were extracted from the full text papers by two independent reviewers (L. H. and H. F.), using a predefined form. The data collection form contained information on study characteristics (e.g., authors, year of publication), design and methods (e.g., population characteristics, and eligibility criteria), outcome (e.g., type of outcome and outcome assessment), analysis and results (e.g., outcome measures), and conclusions.

Results

Search Findings

Literature searches were finally performed on October 26th, 2017. This search resulted in 587 references, which are shown in Table 1. The detailed process of the study selection followed the PRISMA guidelines and is shown in Figure 1. After removing duplicate references in EndNote, the number of studies was lowered to a total of 309 references (see for more details Table 1; Appendix). Of these, 206 references were excluded based on their titles and abstracts. The remaining 103 studies were further retrieved for a detailed evaluation. A total of 20 studies finally met the inclusion criteria. These selected studies were quite heterogeneous in their design and methodology. The NF therapy protocol as well as the duration, frequency, and number of sessions varied between studies. This will be shown in more detail in Tables 2, 3, and 4.

The 20 results were divided into the following main subjects for ASD: effectiveness, randomized controlled trials, with control condition such as waitlist or placebo/sham-NF or with a control condition such as another therapy (medication or psychotherapy). In the following section, an overview of 20 studies concerning the effectiveness of NF for children with ASD will be given. These studies are presented in more detail in Tables 2, 3, and 4. Table 2 shows three RCT studies, Table 3 shows 13 non-randomized controlled studies and Table 4 summarizes four experimental studies. The efficacy of NF for different subtypes of ASD will be mentioned and an overall conclusion will be given.

Effectiveness of Neurofeedback Therapy

Overall, all studies except one (Scolnick, 2005), report positive outcomes of NF for children with ASD (see Tables 2–4). In one study, NF therapy was found to lead to a significant relieve in symptoms within 89% of the participants

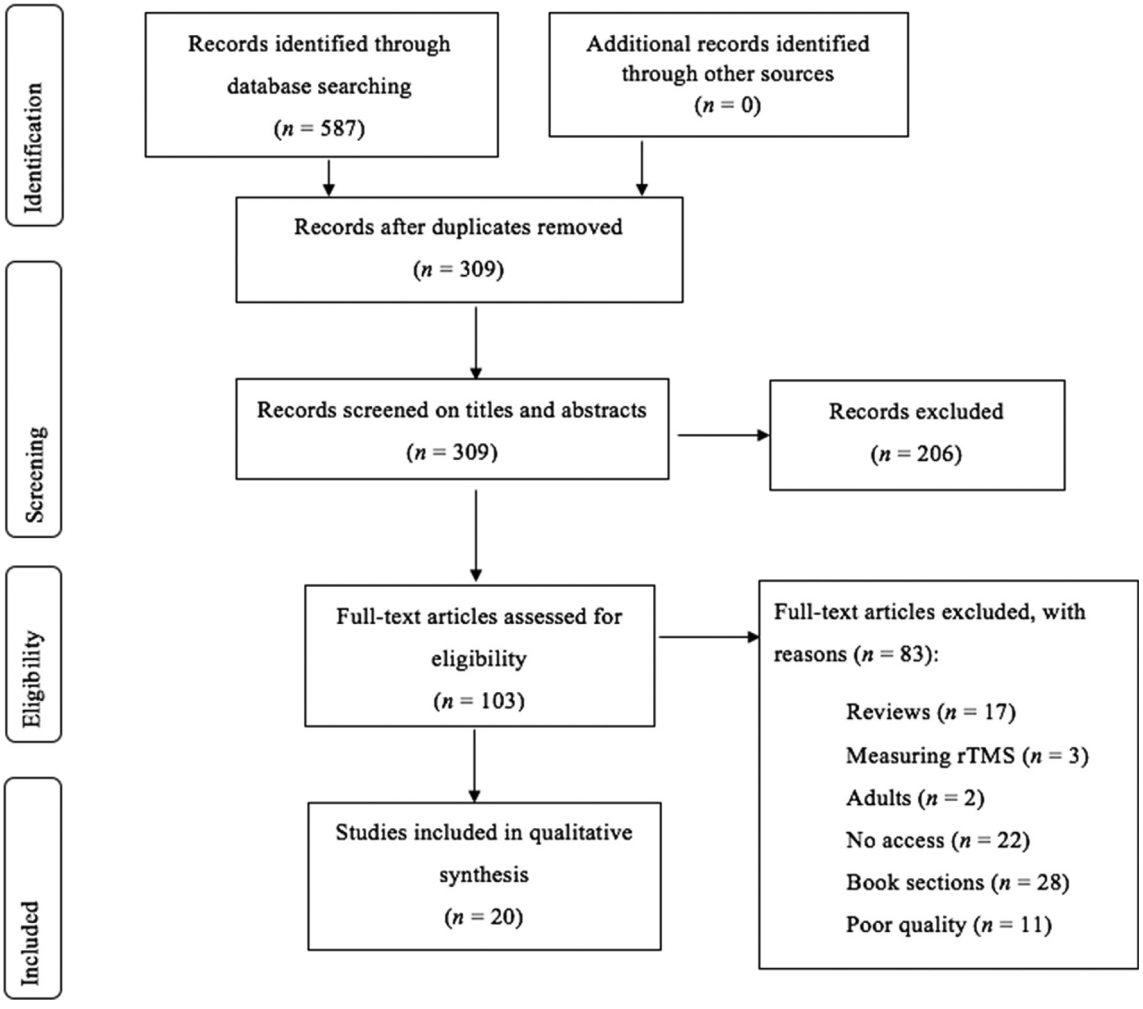

Figure 1. PRISMA flow diagram of identification and selection of eligible studies.

Table 1. Results for searches performed on October 26th, 2017

Databases	References
Embase.com	181
Medline Ovid	72
Web of science	120
Cochrane CENTRAL	9
PsycINFO Ovid	105
Google scholar	100
Total	587
References without duplicates	309

(Coben & Myers, 2008). Pineda and colleagues (2008) found mostly positive outcomes and also reported one important side-note after conducting two studies. In the first study, 80 high-functioning ASD participants were assigned to an experimental training of mu frequency band (8–13 Hz) or placebo condition. The experimental training led to more coherence in brain patterns and increased, as well as sustained attentional capacities in subjects. To address some issues (e.g., the lower frequency band in Study 1), a second study was carried out. In the second study, 19 high-functioning ASD children underwent a similar procedure on high mu band (10–13 Hz) and also showed prolonged sustained attention. However, no improvements in the ability of imitation could be observed in the participants following the training. In addition, in this study, parent ratings of sensory and cognitive awareness decreased. Therefore, authors reported the side-note that NF may improve certain symptoms while worsening others.

Children with ASD symptoms are often faced with great barriers in social interactions (American Psychiatric Association, 2013). In total, seven studies specifically reported improvements of social behavior in children with ASD due to NF therapy (Datko, Pineda, & Müller, 2018; Friedrich et al., 2015; Jarusiewicz, 2002; Kouijzer, de Moor, Gerrits, Congedo, & van Schie, 2009; Kouijzer, van Schie, de Moor, Gerrits, & Buitelaar, 2010; Pineda, Carrasco, Datko, Pillen, & Schalles, 2014; Zivoder, Martic-Biocina, Kosic, & Bosak, 2015). These improvements (i.e. social

Table 2. Overview of randomized controlled studies on the efficacy of NF for ASD

Author (year)	*N*, (participants and condition)/control group), (% male) age range	Target condition	NF protocol, number of sessions per week (pw), duration (min.) and total amount	Control condition, *N*, randomization (if stated), mean age	Collateral treatment allowed	Blinded condition	Instruments of measurements	Results
Pineda et al. (2008)	Study 1: 7, (4/3), (84%), mean = 9.8 years, IQ ≥ 80	Autism, high-functioning	Study 1: mu-alpha/beta NF & EMG feedback, 3 pw, 30 min, 30 total	Study 1: (*n* = 3), randomized sham-NF	na	No	Study 1: qEEG, neuropsychological tests of cognition, attention, and behavior (ATEC, MSI, TOVA)	Study 1: NF increased brain frequency and coherence, increased sustained attention ability, and ATEC ratings.
	Study 2: 19, (9/10), (84%), mean = 9.8 years, IQ ≥ 80		Study 2: high mu-alpha/beta NF	Study 2: (*n* = 10), randomized sham-NF			Study 2: qEEG, Neuropsychological tests on (ADOS, ADI-R, ATEC, MSI, TOVA, WASI)	Study 2: NF improved brain frequencies coherence and normalization, improved sustained attention and ATEC rating.
Kouijzer et al. (2010)	20 (10/10), (85%), mean = 9.3 years, IQ ≥ 80	ASD (Autism, Asperger, PDD-NOS)	Theta-NF, 2 pw, 40 total	Waitlist, (*n* = 10), randomized	No	No	Parent ratings of social and communicational skills (SCQ, SRS, CCC-2), qEEG, and neuropsychological tests for executive functioning and attention (TOSSA, TMT, TOL, Stroop)	NF reduced theta by 60%, modulated ACC activity and improved significantly reciprocal social interactions and communication skills.
Kouijzer et al. (2013)	38 (13/12/13), (77%), mean = 15 years, IQ ≥ 80	ASD (Autism, Asperger, PDD-NOS)	19-Channel theta/delta EEG-NF, 2 pw, na, 40 total	SC-biofeedback (*n* = 12) (75%), *M* = 14 years; and waitlist, (*n* = 13)(85%), *M* = 15 years	na	Blinded for NF or SC feedback group, but not for waitlist condition.	Parent ratings of social and communicational skills (SCQ), qEEG, and neuropsychological tests on cognitive flexibility and planning (CGI, Stroop, TOL, TOSSA, TMT, WISC-III)	NF significantly improved delta and theta in 54% of subjects. NF improved cognitive flexibility, but not significantly. NF was due to non-specific factors.

Notes. ADOS = Autism Diagnostic Observation Schedule; ADI-R = Autism Diagnostic Interview; ASD = Autism Spectrum Disorder; ATEC = Autism Treatment Evaluation Checklist; CPT = Continuous Performance Test; CCC-2 = Children's Communication Checklist; CGI = Clinical Global Impressions; MSI = Magnetic Source Imaging; PDD NOS = Pervasive Developmental Disorder Not Otherwise Specified; SCQ = Social Communication Questionnaire; SRS = Social Responsiveness Scale; TOSSA = Test of Sustained Selective Attention; TMT = Trail Making Test; TOL = Tower of London; TOVA = Test of Variables of Attention; qEEG = quantitative Electroencephalogram; VABS = Vineland Adaptive Behavior Scale; WASI = Weschler Abbreviated Scale of Intelligence; WISC-III = Wechsler Intelligence Scale for Children, Third Edition.

Table 3. Overview of non-randomized, controlled studies about the efficacy of NF for ASD

Author (year)	*N* (participants and condition)/control group), (% male), age range	Target condition	NF protocol, number of sessions per week (pw), duration (min), and amount of sessions	Control group	Collateral treatment	Blinded condition	Instruments of measurement	Results
Jarusiewicz (2002)	24 (12/12), (92%), 4–13 years	ASD	Individualized NF; 1–3 pw; 30 min; 20–69 total	Waitlist, (*n* = 12), (92%), 4–11 years, matched	na	No	Neuropsychological tests and parent ratings on behavior categories (ATEC, FEAS, Othmer Assessment)	NF reduced symptoms by 26%. Parents rated NF to improve all behavioral categories: socialization, vocalization, anxiety, schoolwork, tantrums and sleep. Improvement was independent of initial symptom severity.
Coben and Padolsky (2008)	37, (na), na	ASD (= 56.8% PDD-NOS; 18.9% Autism; 13.5% Asperger; 10.8% Childhood Disintegrative Disorder)	Individualized NF for hyper-connectivity; 2 pw; min na; 20 total	Waitlist (*n* = 12), with ASD, matched	No	No	Parents rated executive functioning, behavior, adjustment (ATEC, BRIEF, GADS, GARS, PIC-2), qEEG, IR (measuring rCBF), and neuropsychological tests for attention, visual perception, executive function, and language (na)	NF improved symptoms with 89% success rate significantly. Symptom reduced 40%, hyper-connectivity reduced by 76%.
Kouijzer, de Moor, Gerrits, Buitelaar, and van Schie (2009)	14, (86%), 8–12 years, IQ $\geq$ 70	ASD (PDD-NOS)	Standardized Theta/beta NF on right hemisphere; na; na; 40 total	Waitlist, (*n* = 7), matched	No	No	Parent ratings for social interaction, communication and behavior (CCC-2, Auti-R), qEEG, and neuropsychological tests for executive functioning (na)	NF improved executive functioning, reduced theta and delta, and increased beta.
Coben and Myers (2010)	37 (25/12), (84%), 3.92–14.66 years, mean = 8.92 years	ASD (*n* = 7 Autism; *n* = 21 PDD-NOS; *n* = 4 CDD; *n* = 5 Asperger)	NF based on regions of maximal hyper-connectivity; na; 20 (37) total	Control group (*n* = 12; 83% male), matched for age, gender, race, handedness, other treatments, severity of symptoms	Yes, not specified	No	ATEC, GADS, GARS, BRIEF, PIC-2, QEEG	ASD patients improved significantly with NF treatment compared to waitlist. NF findings included 40% reduction in core ASD symptomatology which was associated with 76% decreased hyper-connectivity.

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Table 3. (Continued)

Author (year)	*N*, (participants and condition)/control group), (% male) age range	Target condition	NF protocol, number of sessions per week (pw), duration (min), and amount of sessions	Control group	Collateral treatment	Blinded condition	Instruments of measurement	Results
Silva et al. (2016)	30 (10/10/10)	Autism (*n* = 10), intellectual impairments (*n* = 10), non-autistic (n = 10)	NF; na, 10 min, na	Control group	na	No	EEG signals	For all groups, the stimulation process produced additional activation in the neural area under study.
Liu et al. (2017)	4 (2/2)	ASD, high functioning (*n* = 2)	fNIRS-based NF; 5 total	Control sham-feedback (*n* = 1)			Facial-identity recognition training program	Subjects who received real-FB showed more improvement in facial recognition performance compared with those receiving sham-FB, particularly in the participant with ASD.
Scolnick (2005)	10, (100%), 12–16 years	Asperger	Individualized NF theta/beta; 2 pw; 30 min; 12–24 total	No*	Medication (na)	No	qEEG, Parent and teacher ratings of behavior (na)	NF improved behavior and led to a trend of normalization of brain frequencies but did not reach significance.
Drysdale, Martinez, and Thompson (2012)	37 (11/3/23), (82%, 67%, 56%), 10–14 years	Asperger (*n* = 14)	SMR/theta NF; na; na; 40 sessions	Control group I: ASD (*n* = 3): 4 sessions NF; Control group II: no NF (*n* = 23)	na	No	MAACL-R	Children with AS who had more than 40 sessions of NF responded the same way to the reading materials as the normally functioning controls with increases in positive affect and decreases in negative affect. Children with AS with less than 4 sessions of neurofeedback did not display this change.
Pineda et al. (2014)	28 (17/11), (76%) mean = 13 years	High-functioning ASD	Mu-rhythm NF theta/beta; 2 pw; 30 min; 40 total	Waitlist, (*n* = 11), (64%), mean = 11 years, matched, healthy, 8–17 years	na	No	Parent rating (ATEC, SRS) and fMRI imitation and observation task	NF increased activation in the human mirror neuron system and improved behavioral ratings, all significantly.
Steiner et al. (2014)	10 (na), 7–12 years, IQ $\geq$ 80	ASD with comorbid attention deficits, language delay, anxiety, sensory integration disorder	Theta/beta; 50 min; 40 total	No*	na	No	Parent ratings (CRS 3-P, ASRS, CARS, CPT, PERMP) and EEG measurements	NF led to significant improvements on 2 out of 3 subscales of ASRS, and improved significantly academic rates (PERMP). Higher motivated subjects showed higher success rates.

(Continued on next page)

Table 3. (Continued)

Author (year)	*N*, (participants and condition)/control group), (% male) age range	Target condition	NF protocol, number of sessions per week (pw), duration (min), and amount of sessions	Control group	Collateral treatment	Blinded condition	Instruments of measurement	Results
Zivoder et al. (2015)	10, (70%), 4–7 years	High-functioning ASD (with communication deficit)	Individualized delta/theta NF; na; 15–20 min; 40–60 total	No*	na	No	EEG, structured interview and parent ratings of behavior, attention, sensory motor skills (na)	NF improved behavior (less aggressive, more cooperation, better communication), attention span and sensory motor skills significantly.
Datko et al. (2018)	28 (17/11), (76%/64%), 8–17 years	ASD, high-functioning	SMR mu-rhythm-based NF; right sensorimotor; theta/beta; 45 min; 40 total	Control group (n = 11)	na	No	ATEC, SRS, fMRI	ASD participants showed increased activation of the human mirror neuron with NFT, with interaction between group (ASD vs. controls) and training (pre- vs. posttraining). Patients also showed behavioral improvements.
Kouijzer, de Moor, Gerrits, Congedo, et al. (2009)	14 (7/7), (86%), 8–12 years, IQ $\geq$ 70	ASD (PDD-NOS)	Standardized Theta/beta NF on right hemisphere; na; na; 40 total	Control group, (n = 7), matched	No	No	Parent ratings for social interaction, communication and behavior (CCC-2, Auti-R), qEEG, and neuropsychological tests for executive functioning (na)	NF executive functioning and social behavior improvements were maintained and increased after 12 months.

Notes. ASD = Autism Spectrum Disorder; ASRS = Autism Spectrum Rating Scale; Auti-R = Scale for early Autism Symptoms; BRIEF = Behavior Rating Inventory of Executive Function; CCC-2 = Children's Communication Checklist; CRS 3-P = Conners Rating Scale-Parent; CPT = Continuous Performance Test; FEAS = Functional Emotional Assessment Scale; fMRI = Functional Magnetic Resonance Imaging; fNIRS = Functional Near-Infrared Spectroscopy; GADS = Gilliam Asperger's Disorder Scale; GARS = Gilliam Autism Rating Scale; IR = Infrared imaging; MAACL-R = Multiple Affect Adjective Check List-Revised; NFT = Neurofeedback Therapy; NF = Neurofeedback; PDD NOS = Pervasive Developmental Disorder Not Otherwise Specified; PERMP = Permanent Product Measure of Performance; PIC-2 = Personality Inventory for Children; rCBF = regional Cerebral Blood Flow; SMR = Sensory-Motor Rhythm; SRS = Social Responsiveness Scale; WISC-III = Wechsler Intelligence Scale for Children, Third Edition.

Table 4. Overview of non-randomized, non-controlled studies about the efficacy of NF for ASD

Author (year)	*N* (participants and condition)/control group), (% male), age range or mean age	Target condition	NF protocol, number of sessions per week (pw), duration (min), and total amount	Control condition	Collateral treatment allowed	Blinded condition	Instruments of measurements	Results
Friedrich et al. (2015)	13, (6/7), (84%/100%), 6–17 years	ASD	Bidirectional NF of theta/beta, 2–3 pw, 60 min, 16 total	No*	na	No	In between measurements of the Social Mirroring Game, neuropsychological tests of, for example, intelligence (ADOS, ASDS, ADI-R, ATEC, CARS, GARS, GADS, SRS, VABS, WISC-III)	NF improved increasing mu rhythm, emotional responsiveness (emotion recognition and spontaneous imitation), and behavior.
Knezevic, Thompson, and Thompson (2010)	19 (84%), 7–21 years	Asperger	SMR/Theta NF, na, 50 min, 40 sessions	No	No	No	TOVA, IVA-CPT, TOL	Participants increased in planning, problem solving inhibition, and shifting and were less impulsive.
Wang et al. (2016)	18 (78%), mean 13.2 years	Asperger (*n* = 14), Autism (*n* = 4)	Prefrontal NF, 1 pw, 25–30 min, 18 total	No	Medication status, dosage, and other variables of pharmacotherapy were accurately monitored and recorded, but were not used as a part of the patients' demographic descriptive characteristics	No	ABC	A linear decrease of theta/beta ratio and relative gamma activity was found.
Hemmati et al. (2016)	26 (na), 5–18 years	ASD	NF, 2 pw, 30–45 min, 40 total	No	na	No	CARS	The average of theta (low frequency) power decreased, but there was no difference in the activity of gamma waves (High frequency).

Notes. ABC = Autistic Behavior Checklist; ADOS = Autism Diagnostic Observation Schedule; ADI-R = Autism Diagnostic Interview; ASDS = Asperger's Syndrome Diagnostic Scale; ATEC = Autism Treatment Evaluation Checklist; CARS = Childhood Rating Scale; GADS = Gilliam Asperger's Disorder Scale; GARS = Gilliam Autism Rating Scale; IVA-CPT: intermediate Visual And Auditory Continuous Performance Test; SMR = Sensory-Motor Rhythm; SRS = Social Responsiveness Scale; TOL = Tower of London; TOVA = Test of Variables of Attention; qEEG = quantitative Electroencephalogram; VABS = Vineland Adaptive Behavior Scale; WISC-III = Wechsler Intelligence Scale for Children, Third Edition.

awareness and communication) were maintained and increased after 1 year follow-up (Kouijzer, de Moor, Gerrits, Congedo, et al., 2009; Kouijzer et al., 2010). Another study demonstrated NF to improve the level of daily functioning (attention, behavior and sensory motor skills) in 10 relatively young children, ranging from 4 to 7 years old (Zivoder et al., 2015). After treatment, all children were reported to be less aggressive, more cooperative, show better communication skills, have a greater attention span, and better sensory motor skills.

However, findings of these studies must be interpreted carefully, as the sample sizes of these studies were quite small (ranging from $n = 10$ to $n = 28$).

Long-Term Effects of Neurofeedback Therapy

This review found two RCT studies concerning the longitudinal effects of NF for ASD in children (Kouijzer et al., 2010; Kouijzer, van Schie, Gerrits, Buitelaar, & de Moor, 2013). One study (Kouijzer, de Moor, Gerrits, Congedo, et al., 2009) found significant maintenance and further increasing improvements in social behavior and executive function at 1 year follow-up. Parents reported significant improvements in social awareness and social communication. These improvements endured 6 months post-treatment (Kouijzer et al., 2010). Another study (Kouijzer et al., 2013) demonstrated that, although NF did not significantly reduced ASD symptoms, it did improve cognitive flexibility, which was maintained at 6 months follow-up.

Discussion

The main goal of this review was to present a comprehensive overview of studies concerning NF for the treatment of children with ASD. In this review, 16 of the 17 non-randomized controlled and experimental studies reported NF to be effective for treating ASD. However, studies also reported that specific functions improved while other functions did not, or even got worse (Pineda et al., 2008). As children with ASD could potentially benefit from this NF treatment, more research for this especially heterogenic group of disorders needs to be conducted. Especially studies that report NF to lead to social improvements are very promising for this broad population. It remains unclear what the exact reason is for the study (Scolnick, 2005) that did not found significant effects, this might be due to the high drop-out (5 out of 10).

As NF influences neurophysiological activity, it is noticeable that NF seems to lead to a transfer of learned skills to social interactions in everyday life. Improvements are found in social behavior (i.e., social awareness and communication), attention and sensory motor skills. That 19 of 20 referenced studies found NF to be effective for ASD is promising, because this population is often faced with severe obstacles in daily life and limited options of treatment.

Strengths and Limitations

While the review findings are novel, several limitations have to be taken into account when interpreting the results. First, due to choices in syntax strategy and single-handedly picking references in EndNote from a large number of studies (587), important studies might have been missed. Second, there is a lack of qualitatively good studies, which makes it hard to draw strong conclusions. Third, many studies applied different NF protocols, which makes it difficult to compare those studies.

Additionally, a previously hidden question was revealed as a result of this review. As can be seen in Tables 2–4, almost all studies report findings on samples consisting of more boys than girls. To our knowledge, only one study addressed this gender question directly and reported NF effects for mathematical disabilities to be found only in boys but this was not discussed in a specific relation to ASD (Hashemian & Hashemian, 2015). As was explained in the introduction of the review, ASD is more common in boys than girls with a ratio of 4:1 (Fombonne, 2005). Therefore, more research should address the possibly different effects of NF on gender in relation to ASD.

Future Directions

Although this review brought several insights in the efficacy of NF for ASD in children, some other aspects remain unclear. For example, there seems to be no clear guidance as to how many sessions of NF are needed for optimal results. Since many areas of neurological dysregulation are implicated with disorders of the autism spectrum, the length of NF treatment is often long (sometimes over 60 sessions). Studies included in this review reported numbers of sessions ranging from 5 to 69 (Jarusiewicz, 2002; Liu et al., 2017). Five sessions were proven to be effective in one study (Liu et al., 2017), whereas any additional improvement could not be found after 4 sessions in another study (Drysdale et al., 2012). However, the authors of the latter study did show that children with ASD who had more than 40 sessions of NF responded the same way as normally functioning controls. Optimal amount of sessions of NF is an interesting aspect to specify, considering that short-term NF would be a valuable and cost efficient tool. However, as NF is based on operant learning principles it would only be logical to assume that symptoms would

improve as more repetitions occur (Vollebregt, Dongen-Boomsma, Buitelaar, & Slaats-Willemse, 2014).

This review found that alpha, beta, theta, and delta waves can be utilized in different ratios in the treatment of ASD (see Tables 2–4). There is currently no firm agreement on optimal treatment protocols. Comparing studies that apply different protocols make it difficult to draw valid conclusions. Though, a specific protocol for Asperger's disorder was offered (Thompson & Thompson, 2003). It involved beta training at 13–16 Hz at T6 (temporal lobe, right side) set to decrease any dominant slow wave activity. A recent study showed that sensorimotor mu-NF has significant positive effects on social behaviors (Datko et al., 2018). This could be an explanation why two mentioned RCTs found significant results, because their training also focused on the sensorimotor region (SMR) of the brain (Kouijzer et al., 2010; Pineda et al., 2008). This might also explain the lack of clinical benefit in the last study from Kouijzer and colleagues (2013), because they omitted the SMR/Beta band from their training. However, future research should continue examining which NF protocol is efficient for which symptom.

Furthermore, if NF effects are correlated with duration of ASD treatment in general, then future research should examine the possibility of a patient-directed model of the treatment (minimal therapist contact). NF is traditionally given in a therapist-directed model, which makes it costly and almost non-manageable for the patient. Almost two decades ago, a patient-directed (which means less involvement of the therapist) model of NF has already been proven to be both feasible and effective (Rossiter, 1998). In addition, NF is found to be effective at home when used in others disorders (Rossiter, 1998) or in a school-setting (Steiner et al., 2014). Future research could support whether NF can also be used this way in ASD. Also, motivation could be a moderating effect of NF therapy. One study (Steiner et al., 2014) regarding patients with Asperger's reported that highly motivated participants showed higher success rates of the treatment than lower motivated participants. More randomized controlled studies should further explore the possible impact of other factors of NF treatment success.

As can be seen in Tables 2–4, almost all studies report findings on samples consisting of more boys than girls. The percentage of male participants reported by studies ranged from 76% (Pineda et al., 2014) to as high as 92% (Jarusiewicz, 2002) and even 100% (Scolnick, 2005). However, no study addressed this gender question directly. Therefore, more research should address the possible influence of gender in the effectiveness of NF in ASD.

Concerning NF for ASD the current literature contains too few controlled studies. Because of this lack of qualitatively good studies we cannot definitely conclude that there is a robust success of NF in ASD. However, several studies concerning NF for ADHD have successfully implemented double-blinded trials, suggesting that this approach is feasible (Micoulaud-Franchi et al., 2014; Strehl et al., 2017). We therefore suggest future research to also implement double-blinded trials of NF for ASD and contribute to the existing literature.

Future research should also focus on a combination of EEG and rtfMRI neurofeedback. Several studies suggest potential application of simultaneous hemodynamic (rtfMRI) and electrophysiological (EEG) neurofeedback in the development of novel cognitive neuroscience research paradigms and enhanced cognitive therapeutic approaches for major neuropsychiatric disorders (Caria & de Falco, 2015; Zotev, Phillips, Yuan, Misaki, & Bodurka, 2014). Hitherto, the knowledge about application of EEG-rtFMRI neurofeedback in ASD is very limited. Additionally, authors would like to encourage researchers of future publications to engage in prospective registrations of trial registries with respect to publication bias. As modeling methods are difficult to implement and require lengthy calculations, these efforts succeeded the realm of this review.

Conclusion

Concerning NF for ASD in children, the current literature review shows promising results, but contains too few controlled studies. In conclusion, the existing literature to date provides reason for optimism for NF being a valuable alternative treatment for ASD. This is promising and can especially be recommended for non-responders or children that respond not effectively to medication. An important advantage of NF compared to pharmacological therapy is that there are no side-effects. An advantage of NF compared to behavioral therapy is that it can be more cost-effective, when using the patient-directed model. NF treatment could be improved by personalized (EEG-guided) protocols, focused on individual differences and symptoms. More research should be conducted, as these patients are often very young in age and dependent on evidence-based therapies of high quality with no aversive effects.

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Appendix

Embase.com (181 results)

(neurofeedback/exp OR (("feedback system"/de OR "virtual reality"/exp OR "computer assisted therapy"/de) AND (electroencephalogram/exp OR electroencephalography/exp)) OR (neurofeedback* OR ((eeg OR brainwave OR brain-wave OR QEEG OR electroencephalogra* OR alpha OR beta OR gamma OR delta OR theta OR Psychophysiol* OR interaction* OR neuro* OR operant*-condition*) NEAR/6 (feedback OR biofeedback*)) OR ((operant*-condition* OR reward*) NEAR/6 (eeg OR electroencephalogra* OR electromyogra* OR emg))):ab,ti) AND (autism/exp OR (autis*):ab,ti)

Medline Ovid (72 results)

(neurofeedback/ OR (("feedback"/ OR exp "Feedback, Physiological"/ OR "Virtual Reality Exposure Therapy"/ OR "Therapy, Computer-Assisted"/) AND (exp Electroencephalography/)) OR (neurofeedback* OR ((eeg OR brainwave OR brain-wave OR QEEG OR electroencephalogra* OR alpha OR beta OR gamma OR delta OR theta OR Psychophysiol* OR interaction* OR neuro* OR operant*-condition*) ADJ6 (feedback OR biofeedback*)) OR ((operant*-condition* OR reward*) ADJ6 (eeg OR electroencephalogra* OR electromyogra* OR emg))).ab,ti,kf.) AND (Autistic Disorder/ OR (autis*).ab,ti,kf.

PsycINFO Ovid (105 results)

(Neurotherapy/ OR (("feedback"/ OR "Virtual Reality"/ OR "Computer Assisted Therapy"/) AND (exp Electroencephalography/)) OR (neurofeedback* OR ((eeg OR brainwave OR brain-wave OR QEEG OR electroencephalogra* OR alpha OR beta OR gamma OR delta OR theta OR Psychophysiol* OR interaction* OR neuro* OR operant*-condition*) ADJ6 (feedback OR biofeedback*)) OR ((operant*-condition* OR reward*) ADJ6 (eeg OR electroencephalogra* OR electromyogra* OR emg))).ab,ti.) AND (Autism Spectrum Disorders/ OR (autis*).ab,ti.)

Cochrane CENTRAL (9 results)

((neurofeedback* OR ((eeg OR brainwave OR brain-wave OR QEEG OR electroencephalogra* OR alpha OR beta OR gamma OR delta OR theta OR Psychophysiol* OR interaction* OR neuro* OR operant*-condition*) NEAR/6 (feedback OR biofeedback*)) OR ((operant*-condition* OR reward*) NEAR/6 (eeg OR electroencephalogra* OR electromyogra* OR emg))):ab,ti) AND ((autis*):ab,ti)

Web of Science (120 results)

TS=(((neurofeedback* OR ((eeg OR brainwave OR brain-wave OR QEEG OR electroencephalogra* OR alpha OR beta OR gamma OR delta OR theta OR Psychophysiol* OR interaction* OR neuro* OR operant*-condition*) NEAR/5 (feedback OR biofeedback*)) OR ((operant*-condition* OR reward*) NEAR/5 (eeg OR electroencephalogra* OR electromyogra* OR emg)))) AND (autis*))

Google Scholar (100 results)

NF "attention Neurofeedback autism|autistic"

