Neurofeedback in autism spectrum disorders

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ABBREVIATIONS

ASD	Autism spectrum disorder
ATEC	Autism Treatment Evaluation Checklist
MNS	Mirror neuron system
QEEG	Quantitative electroencephalography

AIM To review current studies on the effectiveness of neurofeedback as a method of treatment of the core symptoms of autism spectrum disorders (ASD).
METHOD Studies were selected based on searches in PubMed, Ovid MEDLINE, EMBASE, ERIC, and CINAHL using combinations of the following keywords: 'Neurofeedback' OR 'EEG Biofeedback' OR 'Neurotherapy' OR 'Mu-Rhythm' OR 'SMR' AND 'Autism' OR 'Autism Spectrum Disorder' OR 'Pervasive Developmental Disorder'.
RESULTS The existing evidence does not support the use of neurofeedback in the treatment of ASD. Studies with outcomes in favour of neurofeedback might be showing an improvement in comorbid attention-deficit–hyperactivity disorder symptoms rather than a true improvement in core ASD symptoms.
INTERPRETATION Limitations of this review are those inherent in the studies available, including small sample size, short duration, variable diagnostic criteria, and insufficient control interventions, all causing a lack of generalizability.

Autism spectrum disorder (ASD) is an increasingly used clinical umbrella label for the DSM-IV-TR/ICD-10[1,2]-based diagnoses of autism, Asperger syndrome, and atypical autism/pervasive developmental disorders not otherwise specified. In fact, the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders will discard single disorders in favour of the term autism spectrum concept, indicating differing grades of severity of one diagnosis (http://www.dsm5.org). Recent epidemiological studies estimate the prevalence of ASD to be around 1% in the general population. ASD is characterized by a triad of disabling features involving reciprocal social interaction, mutual verbal and non-verbal communication, as well as inflexible, stereotypic thoughts and behaviours. These impairments appear in early childhood, tend to be chronic, and often lead to poor outcome in adulthood,[3] particularly in cases with coexisting intellectual disability, language delay, and genetic/neurological syndromes. Numerous types of intervention – both behaviour orientated and biological – have claimed to generate benefits regarding level of functioning and quality of life for people with ASD, but few have actually been scientifically and systematically investigated.[4] Among the sufficiently evidence-based approaches are early intensive behaviour interventions such as applied behaviour analysis, which has yielded robust positive treatment effects, particularly on IQ in milder forms of ASD. Of the biologically-based treatments, pharmacological intervention with risperidone seems to be useful to ameliorate comorbid symptoms of ASD, especially 'challenging behaviours' involving tantrums, self-injury, and aggressiveness. Psychiatric comorbidity is common and frequent in ASD, and includes attention-deficit–hyperactivity disorder (ADHD), depression, and obsessive–compulsive disorder.[3]

There is a long tradition of using 'alternative' treatments in ASD. However, most of these interventions lack scientific evidence, or have been proven to be ineffective.[4] Among alternative treatment approaches, neurofeedback has gained increasing attention in recent years as a treatment for children with ASD. Neurofeedback is a form of biofeedback, which itself is based on behaviour therapy aimed at controlling central nervous system activity.

Meta-analytical evidence suggests that neurofeedback may be effective for the treatment of inattention and impulsivity in children with ADHD, a frequent coexisting condition in ASD.[5–7] The evidence for applying neurofeedback as an effective treatment for ASD core symptoms is, however, less consistent.

The objective of this article is to review the theory of and research on neurofeedback in children and adolescents with ASD. Studies were selected based on searches in PubMed, Ovid MEDLINE, EMBASE, ERIC, and CINAHL using combinations of the following keywords: 'Neurofeedback' OR 'EEG Biofeedback' OR 'Neurotherapy' OR 'Mu-Rhythm' OR 'SMR' AND 'Autism' OR 'Autism Spectrum Disorder' OR 'Pervasive Developmental Disorder'. The review is

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divided into three sections. The first section describes the procedure and rationale of neurofeedback usage in ASD, for example the evidence for electrophysiological alterations that are targeted by neurofeedback. The second section comprises a review of ASD neurofeedback studies, highlighting the strengths and limitations of this approach for treating ASD. The last section is devoted to open questions and future challenges regarding the use of neurofeedback in ASD.

What this paper adds

- All available data on neurofeedback in ASD and in comorbid ASD/ADHD are reviewed.
- General and specific methodological issues in research on neurofeedback are discussed.
- Clinical implications/recommendations for the use of neurofeedback in ASD are provided.
- Although existing evidence does not support the use of neurofeedback in ASD, it may hold promise for the treatment of ADHD-like symptoms in ASD.

NEUROFEEDBACK: PROCEDURE AND RATIONALE

Neurofeedback refers to training in self-regulation aiming to achieve control over cortical electrical activity. The aim of neurofeedback training is to teach children with ASD to adapt their neurophysiological profile so that it matches those of typically developing children, resulting in subsequent improvement in symptoms. The self-regulation of cortical activity is realized through a process of operant learning using real-time representation of electroencephalographic (EEG) parameters.

A multitude of animated feedback presentations that are suitable for children and adolescents are currently available. EEG measures of interest are converted into optical or acoustic signals and fed back on a screen in real time. In some feedback animations, the cortical activity is, for example, represented by the height of a feedback object (e.g. a ball or a plane) moving from the left side to the right side of the screen. If the EEG activity is regulated in the desired way, the object rises or sinks. In other paradigms, the colour of an object on the screen, representing the activity of interest, has to be changed. Successful trials are immediately rewarded by a tone, a smiley face, or points that can be gained.[6,7] Individual thresholds of parameters can be adjusted throughout the course of the training so that an encouraging amount of positive feedback is guaranteed.

Like other operant training, neurofeedback requires a transfer from the training context to the everyday life of the individual. Therefore, some training trials without feedback can be incorporated to catalyze generalization. To date, no severe or permanent side effects of neurofeedback have been reported. Headaches and fatigue have been occasionally documented, which seem to be attributable to the attentional demands and associated muscular tension during training sessions.[6]

Electrophysiological alterations in ASD

The increased interest in neurofeedback as a possible treatment tool in ASD can be understood in the light of increasing research elucidating the neurobiological basis of ASD. The present work cannot provide a comprehensive review of electrophysiological investigations in individuals with ASD. Rather, it is limited to describing those distinctive features of the neurobiology of ASD that appear as reasonable targets of neurofeedback treatment.

Spontaneous EEG and spectral parameters

Quantitative electroencephalography (QEEG) applies computerized mathematical algorithms to convert raw EEG data into frequency bands of interest. Traditionally, five wide frequency bands have been studied, typically defined as delta (1.5–3.5Hz), theta (3.5–7.5Hz), alpha (7.5–12.5Hz), beta (12.5–30Hz), and finally gamma (30–70Hz). Each frequency range is averaged across a sample of data and quantified into mean amplitude (i.e. voltage in mV). The absolute and relative power (i.e. percentage of total power) in each frequency band can be calculated. Paediatric EEG differs from adult EEG because of maturation. Whereas decreases in the lower frequency bands take place during the first years of life, increases in the alpha band typically continue until early adolescence, while the beta band continues to mature until adulthood.

QEEG studies have been carried out in various child psychiatric disorders, with ADHD having attracted most attention. Fewer QEEG studies have been conducted in children with ASD. Although the findings have been quite inconsistent in ASD, QEEG research has identified various degrees of alterations in one or more EEG spectral characteristics. Ogawa et al.[8] found an elevated frontal alpha band in ASD, and Cantor et al.[9] found that children with ASD had elevated power in frontotemporal regions, especially in the delta band.

Chan and Leung[10] examined 17 children with ASD and 105 typically developing comparison children in a single-channel QEEG study. Higher absolute sensorimotor rhythm (low beta 12–15Hz activity) and beta amplitudes were the best predictors that correctly discriminated children with ASD from typically developing children. The autistic group was also found to have a significantly higher theta/beta ratio than the typically developing children, although with a small effect size.

In a larger multi-electrode QEEG study including 66 children with ASD and 90 typically developing age-matched comparison children, the same research group detected significantly less relative alpha and more relative delta in children with ASD than in the comparison children.[11] These QEEG characteristics were not regionally specific, but were rather observed across the whole cortex. In contrast to their previous finding, the theta/beta ratio of children with ASD was comparable to that of typically developing comparison children. Coben et al.[12] found an increase in the proportion of relative theta, especially above dorsal brain areas, and a related reduction in absolute beta over the right hemisphere, but an increase in mid-line beta power in children with ASD. Murias et al.[13] reported comparable variations of excess theta and beta in adults with ASD. Whether these findings are specific to ASD and prove to be stable in larger samples is unknown, and the connection to autistic behaviour remains unclear. Methodological differences, such as varying levels of age and adaptive and cognitive functioning in the study participants, and the use of different QEEG measures might be factors contributing

to the discrepant findings. Given the inconsistencies of the QEEG findings and their unknown specificity for ASD, it seems premature to generalize the findings in order to provide a tailored rationale for a QEEG-based neurofeedback protocol in ASD.

Intra- and interhemispheric coordination

The coherence of EEG activity between two cortical sites provides information about the cortico-cortical coupling of brain activity.[14] EEG coherence has not been investigated thoroughly in ASD. The existing evidence is heterogeneous and inconsistent. In addition, the available studies are not sufficiently comparable given the differences in methodology, including age, referencing, and coherence measurements. Nevertheless, some studies point to intra- and interhemispheric communication and coordination malfunctioning in ASD. In a small sample (n=11), Cantor et al.[9] found elevated coherence compared with a comparison group. They concluded that autism may be characterized by a maturational lag in cerebral functioning and a lack of cerebral differentiation.

In the largest trial published to date, Coben et al.[12] compared 20 children with ASD with 20 age-, sex-, and IQ-matched typically developing children. ASD was linked to a pervasive pattern of inter- and intrahemispheric neural underconnectivity, which could be interpreted as an indication of disturbed cortico-cortical communication. In adults with ASD, Murias et al.[13] observed locally restricted hyperconnectivity (especially within the left frontotemporal area) and coincidental reduced coherence between frontal and more distant areas. This might be linked to local information processing rather than global holistic information processing, with the former being said to be predominant in individuals with ASD.[15,16] Moreover, these results are in accordance with evidence from other EEG, magnetic resonance imaging, and functional magnetic resonance imaging studies, which judge aberrations in neuronal connectivity to be an important anatomical correlate of autistic symptomatology. Disconnectivity in ASD seems to be associated with impairment of cognitive functioning,[17] executive dysfunction,[15] and altered processing of emotions.[18] It may, therefore, serve as a rationale for using neurofeedback in ASD.

Altered suppression of the mu rhythm

It has been hypothesized that a dysfunctional mirror neuron system (MNS) underlies ASD. In macaques and humans, mirror neurons are assumed to play an important role not only during execution of relevant motor actions but also during observation of analogous motions of a peer. The MNS might enable individuals to identify the intentions of others by mentally simulating their acts and emotions,[19] potentially forming the basis for language-related constructs such as theory of mind.[20] A growing body of functional neuroimaging and neurophysiological data provides evidence for a link between MNS dysfunction and impaired social cognitive processes such as recognition of emotion, imitation, and action prediction.[21] It is hypothesized that MNS alteration offers an explanation for some of the most striking dysfunctions in ASD: impairments in social reciprocity, lack of cognitive empathy, and poor imitation. Unlike in macaques, MNS activity is measured only indirectly in humans. EEG studies provide indirect, non-invasive access to the MNS function in humans. It has been suggested that the so-called mu rhythm is an electrophysiological indicator of the human MNS. The mu rhythm, an 8–13Hz activity over the sensorimotor cortex, is suppressed if an individual carries out a voluntary movement. Interestingly, in typically developing individuals, the mu rhythm is also suppressed in the absence of actual movements, for example during the imagination, preparation, and observation of motor actions. A lack of mu suppression over the somatosensory cortex has been hypothesized as an electrophysiological correlate of MNS dysfunction.[21] However, empirical studies have yielded conflicting results.[22,23] In individuals with ASD, mu suppression occurs only during self-executed motor actions, and is lacking during observation of another person's movements.[24] Lack of mu suppression might contribute to poor imitation skills in children with ASD.[25] The degree of mu suppression closely correlates with the ability to imitate movements and facial expression[26] and with the degree of intimacy shared with the person observed.[27] Aside from these findings, Pineda and Hecht[28] examined the correlation between mu suppression and accuracy on social perceptual and social cognitive tasks in typically developing adults and concluded that social perceptual tasks are positively correlated with mu suppression. In addition to mu suppression, other electrophysiological correlates of MNS in ASD have been suggested, such as a reduced beta suppression[24] and altered beta power, particularly during observation of others' actions.[21]

In summary, the association between ASD and presumed electrophysiological indicators of MNS dysfunction form a hypothetical rationale for a role for neurofeedback in ASD.

Electrophysiological correlates of comorbid ADHD in ASD

Besides ASD core symptoms, the comorbid symptoms of ADHD in ASD form an indication for neurofeedback in ASD. Studies suggest that 40 to 50% of individuals with ASD suffer from additional ADHD, even though autistic disorders are still considered as exclusion criteria for the diagnosis of ADHD in DSM-IV-TR. As comorbid ADHD symptoms severely influence the clinical appearance of ASD, their treatment within ASD should be obligatory.[29] The fact that the current classification system makes it impossible to diagnose ADHD and ASD simultaneously has led to widespread neglect of research on this issue in the past. This also applies to neurophysiological studies. As a consequence, it remains unclear how individuals with ASD with and without comorbid ADHD differ from each other concerning their EEG profiles. The only study to date that provides hints examined QEEG differences between two groups of children with ADHD, one scoring high, the other low, on a measure of ASD severity. In comparison with the low-scoring group, individuals with prominent autistic features had a number of qualitative differences in the beta and theta bands.[30] Owing to the paucity of studies on comorbid ASD and ADHD, findings from EEG studies in ADHD have to serve as a proxy for QEEG. QEEG

studies using cluster analysis have reported distinct EEG-defined subgroups within ADHD samples (for review, see Barry et al.[31]). Most QEEG studies have reported evidence of cortical hypoarousal. For this subtype, the theta/beta ratio seems to be a reliable measure for differentiating between children with ADHD and typically developing children. Other identified subtypes indicate a maturational lag in central nervous system development and an excess of beta activity (cortical hyperarousal; Table I).

Neurofeedback training protocols

In neurofeedback, protocol refers to 'a specific selection of reinforcement and inhibitory parameters, and the EEG-montage to deliver the training'.[7] In ASD, neurofeedback protocols can be classified into two approaches: the first strategy has the goal of influencing the pattern of EEG frequency bands, while the second aims at increasing mu suppression.

NEUROFEEDBACK STUDIES IN ASD

Case reports

Case reports have observed improvements in both social interaction and attentional function.[32] Scolnick[33] reported only minimal effects and a high dropout rate of 50% in a case series of 10 children with Asperger syndrome.

A large review comprising chart data from 150 children and adults with ASD collected over a period of 15 years was published by Thompson et al.[34] Participants received neurofeedback twice a week, for a total of 40 to 60 sessions. For the majority of participants, feedback was contingent on decreasing theta activity, decreasing beta spindling if present, and increasing fast-wave sensorimotor rhythm (low beta 12–15Hz activity). Neurofeedback was combined with training in metacognitive strategies relevant to social understanding, biofeedback of respiration, electrodermal response, and heart rate variability. The authors report significant improvements in measures of attention as assessed by computerized test batteries and questionnaires, achievement (Wide Range Achievement Test), general intelligence (Wechsler Intelligence Scales), and a 21% reduction in symptoms measured by the Australian Scale for Asperger syndrome.[35] Diagnoses were not assessed in a standardized way, pre- and post-training results were not available for all tests used, and retest effects were not taken into account.

Controlled trials

Studies to date often lack an evidence-based electrophysiological rationale for the selected feedback protocols. For the most part, the diagnostic characterization of the treated samples was

Table I: Studies on electrophysiological alterations in autism spectrum disorders (ASD)

Study	Sample	Outcome in ASD
Spontaneous EEG and spectral parameters		
Ogawa et al.[8]	*n*=21 children with ASD	Elevated frontal alpha; lateralization deficit
Cantor et al.[9]	*n*=11 children with low-functioning autism, three age-matched control groups: typically developing, intellectually disabled, toddlers	Elevated slow-wave power in fronto-temporal regions (especially delta)
Chan and Leung[10]	*n*=17 children with ASD, *n*=105 comparison children	Higher absolute SMR and beta amplitudes, higher theta/beta ratio
Chan et al.[11]	*n*=66 children with ASD, *n*=90 typically developing age-matched comparison children	Less relative alpha and more relative delta; theta/beta ratio comparable to controls
Murias et al.[13]	*n*=18 adults with ASD; *n*=18 controls	Excess theta and beta
Coben et al.[12]	*n*=20 children with ASD, *n*=20 matched typically developing comparison children	Increased relative theta (dorsal) and midline beta, reduced absolute beta (right hemisphere)
Intra- and interhemispheric coordination		
Cantor et al.[9]	*n*=11 children with low-functioning autism, three age-matched control groups: typically developing, intellectually disabled, toddlers	Elevated coherence (less inter- and intrahemispheric asymmetry)
Murias et al.[13]	*n*=18 adults with ASD; *n*=18 comparison children	Locally restricted hyperconnectivity (left fronto-temporal), reduced coherence between frontal and more distant areas
Coben et al.[12]	*n*=20 children with ASD; *n*=20 matched comparison children	Pervasive pattern of inter- and intrahemispheric underconnectivity
Altered suppression of the mu rhythm/electrophysiological correlates of MNS		
Oberman et al.[24]	*n*=10 high-functioning children with ASD and adults; *n*=10 matched comparison children	Lack of mu suppression for observed but not for self-performed actions
Bernier et al.[26]	*n*=14 high-functioning ASD adults; *n*=14 matched typically developing comparison children	Degree of mu suppression closely correlates with the ability to imitate movements and facial expression
Oberman et al.[27]	*n*=13 children with ASD; *n*=13 typically developing comparison children	Greater mu suppression to familiar hands in videos compared with those of strangers
Honaga et al.[21]	*n*=7 individuals with ASD; *n*=10 typically developing comparison children	Reduced post-movement beta rebound following observed but not self-performed actions

EEG, electroencephalography; SMR, sensorimotor rhythm; MNS, mirror neuron system.

unclear or insufficient. A standardized ASD diagnostic process using criterion standard procedures (Autism Diagnostic Interview-Revised; Autism Diagnostic Observation Schedule) and blinded rating has been the exception. There are now five available controlled studies of neurofeedback in ASD. The study by Jarusiewicz[36] was the first study on neurofeedback in ASD with a comparison group design, but had serious methodological flaws. Despite this it has been cited as evidence for the efficacy of neurofeedback in ASD in numerous popular scientific publications. Four different neurofeedback protocols were implemented within this study, which were orientated towards QEEG and the clinical symptomatology of the participants (so-called 'assessment-guided' or 'adaptive' neurofeedback). The rationale for assignment of individuals to a neurofeedback training protocol was neither evidence-based nor sufficiently explicit, but seemed to follow the approach of many (US) neurofeedback centres. Although the author reports the diagnoses of the 40 participants, the diagnostic instruments used are not mentioned. The assignment to the treatment and waiting control group of the participants is unclear: only 12 out of 20 participants completed the 20 neurofeedback sessions. To determine outcome, no last-observation-carried-forward approach was applied. The Autism Treatment Evaluation Checklist (ATEC)[37] was collected to assess core autism. So far, no studies on the reliability and validity of this instrument have been published, and it is not widely used in the autism community. Parental expectations on the efficacy of the treatment were not controlled. These methodological problems substantially limit the findings of an observed reduction in the ATEC overall score of 26% in the training group in comparison with a reduction of 3% within the control group.

The study by Coben and Padolsky[38] applied an 'adaptive' neurofeedback protocol in 37 children, most of them diagnosed with pervasive developmental disorders not otherwise specified. The training aimed to reduce 'local hyperconnectivity' and focused on individual QEEG parameters. A waiting list control group comprised 12 children. Neuropsychological testing for attention and impulsivity as well as an 'infrared measurement' of prefrontal metabolic activity and regional cerebral blood flow were added to the outcome measures. The authors reported a reduction in the overall parent-rated ATEC score of 40% (no significant change occurred in the comparison group) and a decreased hyperconnectivity in 76% of the neurofeedback treatment group. QEEG coherence values were available only for the intervention group, not for the control group.

Recently, Kouijzer et al.[39,40] reported positive short- and long-term effects of QEEG-based neurofeedback training (theta inhibition and low beta enhancement over the right hemisphere) on executive functioning as well as on social interaction and communication skills in ASD. They compared a group of seven children diagnosed with ASD by a child psychiatrist or a clinical psychologist who were receiving 40 sessions of a standard ADHD neurofeedback protocol[41] with a waiting control group with ASD (n=7). Follow-up data were assessed 3 months and 12 months post training. All participants completed a battery of neuropsychological tests on executive function. Significant time by group interactions indicating a superiority of neurofeedback were observed for improvements in auditory selective attention, inhibition capacity, cognitive flexibility, concept generation, and goal-setting capacity. The Children's Communication Checklist (CCC 2-NL) and an adapted version of a Dutch standard autism diagnosis form (parent-report AUTI-R) were used to assess changes in communication and social interaction and other problem behaviour. Parents reported gains in communication and social interaction, and a reduction of problem behaviours following neurofeedback training, while no such differences were found in the control group. The effects of neurofeedback training remained stable at 1-year follow-up.[39] However, parents were not blind to intervention, and thus the effects might be biased by rater expectations. According to the authors, QEEG-based neurofeedback effects may be due to an enhancement of activation within the anterior cingulate cortex, which is the main generator of theta activity. Learnt reduction of theta activity in the anterior cingulate cortex might have led to a normalization of anterior cingulate cortex functioning, including cognitive functions (see Kouijzer et al.[40] for a detailed review of the relation between theta power, anterior cingulate cortex activation, and executive function in ASD).

Pineda et al.[42] have published two neurofeedback studies. The trials aimed to investigate changes in autistic symptoms (especially the ability to imitate) following suppression of the mu rhythm training. In the first study, a small controlled pilot study comprising eight children with high-functioning ASD, the authors reported a 'reactivation' of the previously alleviated mu suppression after 15 sessions of enhancing activity in the range of 8–13Hz above the right sensorimotor region. Findings showed that mu suppression occurred not only during voluntary movements but also during the observation of a stranger's movements. The effect and the improvements in imitation were also detected within the control group. In the second study, in a sample of 19 individuals with high-functioning ASD using a randomized double-blind design, Pineda et al. were unable to replicate the effects on imitation ability despite an improved mu suppression within the treatment group only. Positive effects on autistic symptoms were found using the ATEC. As in the first study, positive effects of neurofeedback on neuropsychological function on the computerized visual continuous performance test (Test of Variables of Attention) were found (Table II).

Effect of neurofeedback on ADHD symptoms

A careful reading of publications on neurofeedback in ASD suggests that reported effects might rather embody an improvement in comorbid ADHD symptoms than a true improvement in autistic core symptoms. However, comorbid ADHD was not reliably assessed, possibly owing to the current exclusion criteria in the classification system that rule out coexisting ASD and ADHD. Because few neurofeedback studies have focused on ADHD in individuals with ASD, we will briefly address the effects of neurofeedback on individuals with ADHD (without comorbid ASD).

Table II: Neurofeedback studies in autism spectrum disorders – controlled trials

Authors	Design	Participants	Treatment	Measures	Outcome
Jarusiewicz[36]	Waiting list comparison group, assignment to groups unclear	*n*=20 children with ASD; *n*=20 waiting list comparison group	20 sessions; 'adaptive' NF oriented towards QEEG and clinical symptoms	ATEC (parent rated)	Reduction of ATEC overall score by 26% (vs 3% in comparison children); only 12 out of 20 participants completed the study; minimal changes in controls
Coben and Padolsky[38]	Waiting list comparison group	*n*=37 children with ASD; *n*=12 matched controls	Individually adapted reduction of 'local hyperconnectivity'	ATEC (parent rated); Gilliam Asperger Disorder Scale, Gilliam Autism Rating Scale, Behaviour Rating Inventory of Executive Function, Personality Inventory for Children; infrared measurement of prefrontal metabolic activity and regional cerebral blood flow	Reduction of ATEC score by 40%, no significant changes in comparison children; improvements on composite measures of attention, visual perception, executive function, and language skills; decreased hyperconnectivity in 76% of treatment group; QEEG not available for comparison children
Kouijzer et al.[39,40]	Waiting list comparison group; 1y follow-up	*n*=7 children with ASD; *n*=7 comparison children	40 sessions of theta inhibition and low beta enhancement	Executive functions: Continuous Performance Test, Verbal Memory Test, Visual Memory Test, Trail Making Test, Milwaukee Card Sorting Test, Wisconsin Card Sorting Test, Tower of London, Symbol Digit Coding; Children's Communication Checklist; parent-report AUTI-R (social interaction, communication, and typical behaviour)	Improvements of auditory selective attention, inhibition capacity, cognitive flexibility, concept generation, goal-setting capacity; improved communication, social interaction, and problem behaviours (parents report); effects stable at 1y follow-up
Pineda et al.[42]	Controlled pilot study	*n*=8 youth with high functioning ASD	15 sessions, enhancing mu suppression (8–13Hz above right sensorimotor region)	Change in mu power in response to observation of movement; Apraxia Imitation Scale; TOVA	Mu suppression not only during own voluntary movements but also during the observation of a stranger's movements; improvements in imitation ability effects also within comparison group
Pineda et al.[42]	Randomized, controlled double-blind design	*n*=19 young people with ASD (verified by ADI-R, ADOS)	–	Change in mu power in response to observation of movement; Apraxia Imitation Scale; TOVA	Improved mu suppression within the treatment group only, no effects on imitation ability; positive effects on visual continuous performance

NF, neurofeedback; QEEG, quantitative electroencephalography; ATEC, Autism Treatment Evaluation Checklist; ADI-R, Autism Diagnostic Interview-Revised; ADOS, Autism Diagnostic Observation Schedule; TOVA, Test of Variables of Attention; AUTI-R, Dutch standard autism diagnosis form.

It can be discerned that data on the effectiveness of neurofeedback on ADHD have clearly improved over the last few years,[5,41,43–45] being about 10 years 'ahead' of the ASD studies in methodological terms. Previous neurofeedback training protocols in ADHD contained frequency band training (theta decrease and beta increase), or training targeting slow cortical potentials, which represent event-related correlates of attention regulation. Within several controlled studies, the short-term improvements achieved through neurofeedback were found to be superior to control interventions both concerning core symptoms and neuropsychological functions. Investigations by Strehl et al.[44] found that the positive effects on ADHD symptoms were stable 6 months post training.

In the first meta-analysis on the effects of neurofeedback on ADHD core symptoms, Arns et al.[5] included data on 467 individuals from 10 prospective controlled trials. Control conditions comprised waiting list groups, interventions such as electromyogram feedback, computerized cognitive training, and stimulant pharmacotherapy. Mean effect sizes (Cohen's *d*) for neurofeedback were 0.81 for inattention and 0.39 for hyperactivity (both assessed via rating scales), and 0.68 for impulsivity as measured by continuous performance tests.

In a first controlled, functional magnetic resonance imaging study on neurofeedback in ADHD, Lévesque et al.[45] reported that the enhancement of sensorimotor rhythm, beta activity, and the suppression of theta activity led to a normalization of key neural substrates of selective attention and response inhibition, i.e. a normalizing effect on the anterior cingulate cortex, caudate nucleus, and substantia nigra. However, lacking an active control condition, it cannot be ruled out that the effects may be explained by unspecific variables of the treatment setting. In summary, based on today's knowledge, one can assume that neurofeedback will henceforth become another component of the treatment of children with ADHD symptoms within the concept of multimodal therapy.[41] However, notably, the UK National Institute for Health and Clinical Excellence guidelines on ADHD do not recommend it as a treatment option.[46]

OPEN QUESTIONS AND FUTURE CHALLENGES

A multitude of methodological limitations will have to be addressed in future studies on neurofeedback in ASD. The use of criterion standard diagnostic instruments and blinded multiple informants using standardized instruments for parents, teachers, and specialists is warranted. The comorbidity of ASD and ADHD needs to be carefully addressed. Established treatment protocols and study designs from ADHD studies should be applied in populations with ASD with additional ADHD symptoms. Follow-up analyses of neurofeedback in ASD to evaluate the long-term effects of neurofeedback intervention and the need for booster sessions are desirable. With regards to health economics, the costs of neurofeedback training need to be calculated and related to effective established forms of ASD treatment. Neurofeedback should be compared with best practice ASD interventions in order to determine its efficacy and effectiveness compared with established techniques. It is unknown today whether neurofeedback adds therapeutic value to existing methods. For instance, a confounding effect of the context of training is conceivable: frequent participation in a structured learning situation alone and contact with a motivated and motivating therapist ('individual tutoring') may lead to effects independent of the neurofeedback training itself. An important limitation of the available studies is their restriction to individuals with ASD with an IQ above 70 ('high-functioning ASD'); this selection bias does not allow for the generalization of current findings to the whole group of children with ASD, which also comprises children with intellectual disability.

In summary, the existing evidence does not support neurofeedback as a treatment that can be recommended for ASD core symptoms. The reviewed studies suggest that neurofeedback protocols that inhibit theta and reward beta activity or sensorimotor rhythm may hold promise for the treatment of ADHD-like symptoms in children with autism.

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