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Neurofeedback for Attention-Deficit/Hyperactivity Disorder (ADHD): A Meta-analysis of Randomized Controlled Trials 'Blinded' and Neuropsychological

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KEY POINTS

Question. Is neurofeedback (NF) an efficacious stand-alone treatment for attention-deficit/hyperactivity disorder (ADHD)?

Findings. We identified 38 randomized controlled trials (RCTs) eligible for meta-analysis. The analyses with *probably blinded* reports and/or neuropsychological outcomes provided no evidence of NF-benefits as a treatment for ADHD. However, two exceptions were noted: small but statistically significant positive effects were observed when the analyses 1) were limited to randomized controlled trials (RCTs) using well-established 'standard' NF protocols and 2) specifically targeted 'processing speed' as an outcome measure.

Meaning. RCTs using *probably blinded* outcomes do not support the use of neurofeedback as a stand-alone ADHD treatment.

ABSTRACT

Importance: Neurofeedback (NF) has been proposed for the treatment of attention-deficit/hyperactivity disorder (ADHD), but the efficacy of this intervention remains unclear.

Objective: To conduct a meta-analysis of randomized controls trials (RCTs) employing *probably blinded* (i.e., rated by individuals probably or certainly unaware of treatment allocation) or neuropsychological outcomes to test the efficacy of NF as a treatment for ADHD in terms of core symptom reduction and improved neuropsychological outcomes.

Data Sources: PubMed (MEDLINE), OVID (PsycInfo, Medline, Embase+Embase Classic), and Web of Science, as well as the reference lists of eligible records and relevant systematic reviews, were searched until 25/7/2023, with no language limits.

Study Selection: We included parallel-arm RCTs investigating NF in participants of any age with a clinical ADHD/hyperkinetic syndrome diagnosis.

Data Extraction and Synthesis: Standardized mean differences (SMDs) with Hedges' g correction were pooled in random effects meta-analyses for all eligible outcomes.

Main Outcomes and Measures. Our primary outcome was ADHD total symptom severity assessed at the first post-intervention time point, focusing on reports by individuals judged probably or certainly unaware of treatment allocation (*probably blinded*). Secondary outcomes were inattention and hyperactivity/impulsivity symptoms and neuropsychological outcomes, post-intervention and at a longer-term follow-up. RCTs were assessed with the Cochrane Risk of Bias 2.0 Tool.

Results. We included 38 RCTs (2,472 participants; aged ~5 to 40-years). *Probably blinded* reports of ADHD total symptoms showed no significant improvement with NF (k=20, n=1207, SMD=0.04, 95%CI[-0.10,0.18]). A small significant improvement was seen when analyses were restricted to RCTs using established standard protocols (k=9, n=681, SMD=0.21, 95%CI[0.02,0.40]). Results remained similar with adults excluded or when analyses were restricted to RCTs where cortical learning/self-regulation was established. Of the five neuropsychological outcomes analyzed, a significant but small improvement was observed only for processing speed (k=15, n=909, SMD=0.35, 95%CI[0.01,0.69]. Heterogeneity was generally low-to-moderate.

Conclusions and Relevance. Overall, NF did not appear to meaningfully benefit individuals with ADHD, clinically or neuropsychologically at the group-level. Future studies seeking to identify individuals with ADHD who may benefit from NF could focus on using standard NF protocols, measuring processing speed, and leveraging advances in precision medicine, including neuroimaging technology.

INTRODUCTION

Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental condition characterized by developmentally-inappropriate, persistent, pervasive, and impairing inattention and/or hyperactivity/impulsivity[1]. ADHD medications, particularly psychostimulants, reduce symptoms and impairment at least in the short-term[2,3], and are recommended as part of multi-modal treatment approaches, including psycho-social therapies and/or psychoeducation programs[3,4].

Neurofeedback (NF) has been proposed as a non-pharmacological treatment for ADHD. It deploys a brain–computer interface to train self-regulation of brain activity using real-time audio/visual feedback of brain activity[5]. Electroencephalogram-based NF (EEG-NF) is the most common, while newer techniques training hemodynamic brain signals for deeper and more focal regulation are being explored (e.g., real time functional Magnetic Resonance Imaging, rt-fMRI-NF; functional Near InfraRed Spectroscopy fNIRS-NF)[6–11]. Two EEG-NF protocols have been used. Frequency band training (FBT) aims to decrease the power of *theta* activity (4-7Hz) and/or increase the *beta* activity (13-30Hz) power to promote attention. Event-related slow cortical potential regulation (SCP) aims to increase/decrease negative potential shifts linked to cortical activation and cognitive preparation[12–15]. Building on evidence from learning theories, such as *operant conditioning* (i.e., implicit learning through reinforcement) or *skill acquisition* (i.e., explicit, goal-directed learning), neurofeedback protocols are premised on the notion that by learning to self-regulate or normalise ADHD-related brain activity, one can alleviate behavioural symptoms and related impairments[13,16].

However, the clinical efficacy of NF as a treatment for ADHD remains disputed despite nearly five decades of research. Randomized controlled trials (RCTs) have often been of poor quality, due to inadequate blinding of treatment allocation (e.g., use of unblinded parent reports or lack of clarity of blinding status), use of non-standardized sub-optimal treatment protocols, and/or failure to assess self-regulation/learning[16–19].

In 2013 the European ADHD Guidelines Group (EAGG) published a meta-analysis, followed by an update published in 2016, of RCTs of EEG-NF in children and adolescents with ADHD[20,21]. A central feature of these meta-analyses was the exploration of the impact of blinding by contrasting two types of ADHD symptom outcomes: i) those reported by individuals "most proximal" (hereafter referred to as MPROX) to the intervention setting and so judged *least likely blinded* (e.g., parent reports on home implemented NF) and ii) those reported by individuals judged at least *probably blinded* (hereafter, PBLIND), either because reports were made under apparently blinded conditions (e.g., placebo-controlled RCT) or by individuals certainly or likely to be unaware of the treatment allocation (e.g., teacher reports where NF was administered in a research clinic/centre). Our 2013 analysis, only powered to analyze ADHD total symptoms, showed a significant NF-related improvement based on MPROX reports (SMD=0.59, 95%CI[0.31, 0.87]), but this effect halved and became nonsignificant with PBLIND reports (SMD= 0.29, 95%CI[0.02,0.61]), suggesting outcome assessor bias. Our 2016 analysis confirmed and extended these findings, showing significant but small NF-related reductions across core ADHD symptoms for MPROX reports (SMDs, 0.26 to 0.36), but not for PBLIND reports (SMDs, 0.06 to 0.17). Further, for RCTs using established 'standard' NF protocols (as defined by Arns et al.

2014, 2020[15,16]), MPROX effects sizes increased (SMD=0.45 to 0.55), but PBLIND outcomes could not be analysed due to insufficient data. NF did not improve neuropsychological functioning. In short, EAGG meta-analytic evidence does not support NF as a stand-alone treatment for ADHD. Broadly similar results have been found in other meta-analyses of 'blinded' RCTs of NF for ADHD[14,22–29].

A considerable number of NF RCTs have been published since the last search conducted by the EAGG in 2015. Many RCTs now include larger samples, longer-term follow-ups, well-controlled designs, and more have PBLIND outcomes. Some have tested the efficacy of rt-fMRI-NF or fNIRS-NF. In the light of this, we present an updated meta-analysis of NF RCTs for ADHD to provide a more accurate and comprehensive estimate of the value of NF as treatment for ADHD in terms of core symptom reduction and improved neuropsychological performance. We also conducted, for the first time, sensitivity analyses with PBLIND outcomes relating to whether effects were stronger; i) when standard EEG-NF protocols were followed and ii) when there was evidence that learning/self-regulation had occurred. We also ran exploratory MPROX analyses to see if novel NF approaches targeting hemodynamic signals of brain activity were efficacious, and to compare NF to medication and other non-pharmacological interventions in head-to-head trials.

METHODS

This preregistered meta-analysis (PROSPERO: CRD42022290005) was reported according to PRISMA 2020 and PRISMA-S[30,31] guidelines (see Supplement 2-3).

Search Strategy

PubMed (MEDLINE), OVID (PsycInfo, Medline, Embase+Embase Classic), and Web of Science were searched until 25/7/23 (see eMethods 3). All articles before this search date were *de novo* screened for eligibility.

Eligibility and selection

We included only peer-reviewed, published parallel-arm RCTs where participants had a clinical ADHD/hyperkinetic syndrome diagnosis as defined by DSM-III/ICD-9 onwards (any subtype/presentation) or with above cut-off scores on validated ADHD rating scales (see eMethods 1 & eMethods 3). DB, SC, and ESB resolved disagreements. Authors of RCTs were contacted for unpublished data/information.

Data extraction

We extracted outcome means and standard deviations at all available time points. Where multiple ADHD outcomes were reported, only one was selected according to a pre-specified hierarchy (see eMethods 4). MPROX outcomes included parent ratings (including when reported by a clinician) if intervention was home-based; teacher ratings if school-based; investigators or clinicians if lab or clinic-based; or self-ratings by adults regardless of intervention setting. PBLIND estimates included reports given by individuals judged as probably unaware of the treatment allocation because of their remoteness from the trial setting, independent observers, or a certainly ‘blinded’ self or parent rating in a RCT with a sham control arm. If multiple PBLIND reports were available, the outcome judged best blinded was selected, i.e., independent assessors (e.g., direct observation) or the most 'remote' assessor from the intervention setting (e.g., teacher over parent if home-based). While MPROX outcomes were, by definition, available from all RCTs with ADHD-related outcomes, fewer PBLIND outcomes were identified. The MPROX and PBLIND outcomes were the same (i.e., from one 'blinded' assessor) for only Alegria et al. (2017)[11,32–34], Baumeister et al. (2018)[35], Bink et al. (2014, 2015, 2016)[36–38], Lam et al. (2022)[9], and Zilverstand et al. (2017)[10].

Data Synthesis

Our primary outcome was ADHD core symptom severity (total combined, i.e., inattention and hyperactivity/impulsivity) measured at the first time point after the final NF session. Secondary outcomes were: inattention and hyperactivity/impulsivity symptoms (separately) or neuropsychological outcomes at the first time point after the final NF session or at a longer-term follow-up assessment (≥3-months and the last follow-up timepoint). Neuropsychological outcomes were grouped as per our previous meta-analysis[39].

Effect size estimates (standardized mean differences, SMDs) were calculated as mean baseline-to-post-assessment (or follow-up) change in the intervention group minus the mean baseline-to-post-assessment (or follow-up) change in the control group divided by the pooled baseline standard deviation, with Hedges' g small sample bias adjustment[40,41]. We conducted random effects models meta-analyses for all outcomes at all available time points (i.e., baseline versus post-assessment or follow-up). SMDs were combined using the inverse variance method[40,42]. Between-SMD heterogeneity was tested using the chi-squared (Q) test, while the magnitude of true versus random heterogeneity was estimated using the I^2 statistic[40]. As in previous EAGG meta-analyses[20,39,43,44], at least five relevant RCTs were required per outcome domain to reduce between-SMD heterogeneity[45].

Sensitivity analyses were conducted to examine NF efficacy: i) for SCP and FBT EEG-NF separately; ii) when an established "standard" protocol was employed (as defined by Arns et al. 2014, 2020[15,16], see eMethods 5); iii) when NF learning was demonstrated (defined as statistically significant change in EEG or hemodynamic patterns in the expected direction); iv) when PBLIND assessments were made in the intervention setting (e.g., direct observation by an independent observer); v) when participants were children/adolescents only (<18-years-old); and vi) when the comparator arms were sham/semi-active controls (e.g., EMG training), placebo tablet, Treatment-as-Usual (TAU), and Waitlist-Control (WLC). Meta-regressions were conducted if at least ten RCTs per predictor (as suggested[46]) were available, with the following predictors: publication year, mean age of sample, % medicated during the treatment period, and overall RoB (low, some concerns, or high)[47]. Additional unregistered exploratory analyses were conducted for; i) RCTs of novel NF targeting hemodynamic signals and ii) head-to-head RCTs comparing NF with a) medication or b) other non-pharmacological treatments.

Publication bias was assessed using Egger's regression test of small study effects, but only for significant results from the main analysis without significant heterogeneity.

Data analysis and data visualisation were conducted in RevMan[42] and the *metafor* package in *R*[48].

RESULTS

Study Characteristics

From an initial 1,457 records, we retained 38 RCTs reported in 53 publications (Total *N* participants = 2,472) (Table 1)[20] (see eFigure 1 for PRISMA flowchart; for included/excluded reports and outcomes, see eMethods 6, eTable1-3). Thirty-three RCTs applied EEG-NF (FBT=24; SCP=8, FBT plus SCP=2). Five applied fMRI or fNIRS. Three studied adults. Nine reported eligible longer-term outcomes (i.e., >3-months after NF was completed; range 6-12-months). Forty-two RCTs were rated as overall “High” risk of bias mainly due to inadequate blinding (eFigure2).

Meta-Analysis Results

We report below the results from our analysis of trials with PBLIND outcomes[9–11,35,49–62] for a more unbiased and robust estimate of NF effects. For fNIRS/fMRI-NF or head-to-head trials, we use MPROX reports due to insufficient PBLIND data (<5 trials). Other analyses of MPROX outcomes are provided in the supplement.

Primary Outcome Measure

There was no significant NF-related improvement on total PBLIND ADHD symptoms (k=20, n=1207, SMD=0.04, 95%CI[-0.10,0.18]; Table & Figure 1; see eFigure 3; eTable 4 for MPROX outcomes) – a finding replicated across nearly all sensitivity analyses (Figure 1; Table 1; eTable 5). A statistically significant but small effect of NF was found in RCTs using standard NF protocols (k=9, n=681, SMD=0.21, 95%CI[0.02,0.40]). Heterogeneity was generally low and non-significant.

Secondary Outcome Measures

ADHD sub-dimensions. There were no significant reductions in PBLIND inattention and/or hyperactivity/impulsivity symptoms (replicated in all sensitivity analyses). Heterogeneity was generally moderate and significant for inattention and low and non-significant for hyperactivity/impulsivity (Figure 1; Table 1; eTable 4-5).

Neuropsychological Outcomes. NF significantly improved speed of processing (k=15, *n*=909, SMD=0.35, 95%CI[0.01,0.69]), but not attention, inhibition, verbal WM, visual WM. Heterogeneity was generally high and significant (Table 2; eTable 6).

Longer-term follow-up outcomes

There were no significant longer-term effects of NF in analyses with all RCTs included (*M*, 6-months; range, 6-12-months; eTable 7-9), with the exception of a significant effect for processing speed (k=8, n=517, SMD=0.32, 95%CI[0.04,0.61]), although this was associated with significant heterogeneity.

Meta-regression

NF effect sizes were generally not significantly predicted by mean age, percentage of medicated participants, publication year, risk of bias, or activeness of comparator arms (eTable 10).

Exploratory Analysis

NF versus other treatments

MPROX reports of ADHD symptoms showed methylphenidate had a significantly greater effect than NF on total ADHD (k=7, n=417, SMD=-0.68, 95%CI[-0.92, -0.44]), Inattention (k=7, n=418, SMD=-0.74, 95%CI[-0.9, -0.52]), and Hyperactivity/Impulsivity symptoms (k=7, n=417, SMD=-0.49, 95%CI[-0.73, -0.26]). There was no significant difference between NF and other non-pharmacological interventions (i.e., cognitive training, physical exercise). All analyses showed low and non-significant heterogeneity (eTable 11). There were insufficient head-to-head trials to analyze PBLIND outcomes.

fMRI/fNIRS

No benefits of fMRI/fNIRS interventions on MPROX reports of ADHD symptoms (Tables 1-2; eTable 4, 7-9). There were insufficient trials to analyze PBLIND outcomes.

DISCUSSION

In the largest meta-analysis of RCTs focusing on at least *probably blinded* neuropsychological outcomes to date, we found no evidence to support the use of current forms of NF as stand-alone treatment for ADHD.

This generally negative picture has two possible exceptions. The first is that established ‘standard’ protocols (as defined by Arns et al. 2014, 2020[15,16]) led to a nominally significant benefit on PBLIND measures of total ADHD symptoms. However, four observations temper the importance of this finding. One, it could be due to the ‘standard’ nature of the protocols or the mixture of different NF approaches that were analysed (FBT v SCP). Two, the small improvement (SMD=0.21) likely falls short of clinical value, and is smaller than what we found in 2016 with only three trials available for analysis (SMD=0.36)[20]. Three, the improvement was not observed in PBLIND measures of inattention or hyperactivity/impulsivity symptoms, separately. Four, the longer-term persistence of this improvement is unclear. Insufficient trials prevented an analysis of longer-term PBLIND outcomes while MPROX outcomes showed no significant improvement. The second exception is that NF improved processing speed, a core neuropsychological component that may underpin higher-order cognitive impairment in ADHD[63,64] – an effect that was also found in longer-term follow-ups. The clinical value of these improvements is questionable as they were barely significant with significant heterogeneity. Furthermore, although effect size estimates were small-to-moderate, they were derived from analyses with multiple dependent effect size estimates (6 out of 15 in the post-assessment analysis; 6 out of 8 in the follow-up analysis) across three RCTs with overlapping comparator samples, potentially inflating the observed effects.

Several of our ‘negative’ findings warrant discussion. First, methylphenidate was superior to NF in alleviating core ADHD symptoms based on MPROX outcomes (but not PBLIND outcomes due to insufficient data). The estimated effect sizes (k=7, SMD range = -0.49 to -0.74, 95%CI range [−0.73 to -0.23]) were similar to meta-analyses of RCTs comparing MPH with placebo in ADHD (SMD range = −0.49 to −0.82, 95%CI range [−1.16 to −0·62])[3], indicating limited clinical benefit of NF. We also found no significant difference between NF and other non-pharmacological treatments (i.e., cognitive training and exercise), suggesting a general ineffectiveness of non-pharmacological interventions for ADHD core symptoms when considering outcomes rated by blinded individuals. This aligns with our recent meta-analytical evidence showing negligible efficacy of cognitive training for ADHD[39]. Second, although no benefits were found with hemodynamic NF techniques (e.g., fMRI, fNIRS), this is based on only 5 trials, therefore further research is warranted given the potential to target deeper, ADHD-relevant brain regions (e.g., opercular right inferior frontal cortex or basal ganglia) with greater spatial (but not temporal) resolution than EEG-based approaches[9]. Third, no significant clinical improvements were found at longer-term follow-ups (i.e., 6-12-months after NF training). Fourth, effect sizes for PBLIND and MPROX outcomes were smaller in the current than in the 2016 meta-analysis (SMD ranges: PBLIND, 0.06—0.15 vs 0.03—0.04 and MPROX, 0.19—0.26 vs 0.26—0.36), but meta-regressions showed no significant relationship between publication year and effect size, suggesting factors other than improved trial design caused this reduction over time.

From a methodological point of view, two findings are noteworthy. First, NF effects did not vary as a function of how active the comparator arm was, as effects were not observed even in trials with less active control conditions. However, the limited number of trials with the least active and non-pharmacological alternative control conditions weakens this conclusion. Second, there was no relationship between whether a RCT established the existence of NF learning and clinical improvement in ADHD symptoms, suggesting that previous evidence of clinical improvement could in this situation potentially result from non-specific, incidental impacts of NF protocols (e.g., wraparound treatment, skill development, or improving tolerance of effortful tasks) rather than self-regulation of brain activity or that the relationship holds only for learning subgroups[65]. However, this interpretation is based only on five RCTs, so the mechanisms driving self-regulation and the individual clinical effects need further investigation.

Given these negative results, what is the future of NF as a treatment for ADHD? First, the limited but significant improvements with 'standard' neurofeedback protocols and in processing speed needs further validation through methodologically sound trials, as this could help refine future approaches targeting higher-order functions[13]. Second, although RCTs provide aggregate-level data, an individualised NF approach could be developed by tailoring NF parameters to individual characteristics. However, reliable baseline indicators (e.g., demographic, neuropsychological or brain function differences) of potential responders to specific training regimes (e.g., SCP training depending on baseline SCPs) are currently lacking[13]. We only had sufficient RCTs to show that baseline medication status did not predict NF effects. Third, combining NF with non-invasive brain stimulation techniques (e.g., repetitive transcranial magnetic stimulation, transcranial direct current stimulation, external trigeminal nerve stimulation) could be potentially fruitful, but evidence supporting their efficacy when applied without NF is limited[66,67] [68]. Finally, incorporating virtual reality or transfer trials (where no immediate feedback is given) could provide a more ecologically valid means to self-regulate symptoms in everyday life, but this approach remains underexplored[69].

As with any meta-analysis, the scope of this one is limited by the trials available for inclusion. First, one in two trials with PBLIND reports measured self-regulation success, so we cannot rule out that the improvements we found might result from non-specific psychological/behavioural effects rather than deliberate training of target brain activity. Testing whether self-regulation occurred and its relation to outcomes should be standard in future RCTs. Second, very few trials measured everyday functioning, quality of life, and academic outcomes, so the impact NF beyond core symptoms and neuropsychological functioning remain uncertain. Third, we could not explore if PBLIND effects were setting-specific, as most trials applied NF in a setting different from the assessment. Fourth, future trials should systematically measure longer-term (i.e., beyond 3-months) effects of NF with PBLIND reports, especially given NF may induce long-term plasticity changes and could have delayed effects[13]. Fifth, most RCTs were judged to have a “high” risk of bias due inadequate blinding. Future studies should be double-blinded and assess blinding integrity. Sixth, as too few trials with PBLIND outcomes from adult samples were available for analysis, future trials should recruit from this age group, although we do not expect major departures from the limited effects we found in younger samples. Seventh, the limited benefit of NF we report raises important questions about the opportunity costs associated with its use and the potential iatrogenic effects from null effects (e.g., disappointment, feelings of lack of control), none of which were considered in the included trials. As recommended when evaluating psychological therapies for ADHD[70], future trials should seriously consider these questions otherwise assessment of the clinical value of NF will remain constrained.

In conclusion, after decades of research, we found no group-level evidence supporting NF as a stand-alone treatment for ADHD. Future studies should therefore weigh the cost-benefits of administering NF over other treatments. Advances in precision medicine, including brain imaging techniques, might eventually identify specific individuals with ADHD for whom NF could be effective and safe.

Conflicts of Interest (alphabetised by surname)

CB has collaborated on projects from the EU Seventh Framework Program and on clinical trials sponsored by Lundbeck, Otsuka, Janssen-Cilag, Angelini and Acadia; **DB** has received grants from FWO (Flanders Research Foundation), KU Leuven, Odisee University College; **TB** Served in an advisory or consultancy role for eye level, Infectopharm, Medice, Neurim Pharmaceuticals, Oberberg GmbH and Takeda. He received conference support or speaker's fee by Janssen, Medice and Takeda. He received royalities from Hogrefe, Kohlhammer, CIP Medien, Oxford University Press; **SB** discloses that he has in the last 3 years acted as an author, consultant, or lecturer for Medice and LinusBio. He receives royalties for textbooks and diagnostic tools from Hogrefe, UTB, Ernst Reinhardt, Kohlhammer, and Liber. He is partner NeuroSupportSolutions International AB; **JB** has been a consultant to / member of advisory board of / and/or speaker for Takeda, Roche, Medice, Angelini, Neuraxpharm, and Servier. He is not an employee of any of these companies, and not a stock shareholder of any of these companies. He has no other financial or material support, including expert testimony, patents, royalties; **DC** reports research funding outside the submitted work from the Australian National Health and Medical Research Council, speaker's fees and honoraria from Novartis, Medice, Servier and Shire/Takeda and royalties from Oxford University Press and Cambridge University Press in the past 3 years; **SC** has collaborated on projects from the EU Seventh Framework Programme, Era-Net Neuron, connect 4 children and on clinical trials sponsored by Lundbeck, Otsuka, Janssen-Cilag, Angelini and Acadia; **FD** has collaborated as sub-investigator in clinical trials sponsored by Lundback and as independent rater in clinical trials sponsored by Servier and Acadia; **MD** received consulting income and research support from Lilly, MEDICE, Shire, Takeda, and eyelevel and research support from the German Research Foundation, German Ministry of Education and Research, German Ministry of Health, and Innovation Fund. He received income as head, supervisor, and lecturer of the School of Child and Adolescent Cognitive Behaviour Therapy at the University Hospital Cologne and as consultant for Child Behaviour Therapy at the National Association of Statutory Health Insurance Physicians (Kassenärztliche Bundesvereinigung). He also received royalties from treatment manuals, books and psychological tests published by Beltz, Elsevier, Enke, Guilford, Hogrefe, Huber, Kohlhammer, Schattauer, Springer, Wiley; **MF** is on the advisory board for Novartis and Neuraxpharm; part of the ISBEA meetings founded by Medice since 2021; **BvdH** receives royalties as one of the editors of "Sociaal Onhandig" (published by Van Gorcum), a Dutch book for parents that can be used in parent training. She is and has been involved in the development and evaluation of several Dutch parent and teacher training programs; has been a member of Dutch ADHD guidelines committees; **CH** has research funded by the National Institute of Health Research (NIHR) and UK Research and Innovation (UKRI); he is an expert Specialist Advisor to the National Institute for Health and Care Excellent (NICE) Medical Technologies Evaluation Programme (MTEP); **JK** has given talks at educational events sponsored by Medice; all funds are received by King's College London and used for studies of ADHD; **PN** has received consultancy fees from Medice, and conference participation support from Medice, Egis Pharmaceuticals and Medis Hungary; DpO. Has received speaker honoraria from

Medice and conference support from HAC Pharma; **SvdO** has received research grants from ZonMw (Dutch Health Research Foundation), FWO (Flanders Research Foundation), KU Leuven and declares a honorarium and reimbursement for travel expenses from MEDICE for being a speaker on non-pharmacological treatments of ADHD. She has been an advisor of the Dutch ADHD Guidelines group, is on the higher heath council in Belgium; an advisory committee to the Belgian Minister of Health on ADHD and is board member of the ADHD advocacy organization in Flanders, Belgium; **JAR-Q** was on the speakers' bureau and/or acted as consultant for Biogen, Idorsia, Casen-Recordati, Janssen-Cilag, Novartis, Takeda, Bial, Sincrolab, Neuraxpharm, Novartis, BMS, Medice, Rubió, Uriach, Technofarma and Raffo in the last 3 years. He also received travel awards (air tickets + hotel) for taking part in psychiatric meetings from Idorsia, Janssen-Cilag, Rubió, Takeda, Bial and Medice. The Department of Psychiatry chaired by him received unrestricted educational and research support from the following companies in the last 3 years: Exeltis, Idorsia, Janssen-Cilag, Neuraxpharm, Oryzon, Roche, Probitas and Rubió; **AS** has received research funding from the Wellcome Trust, and has received royalties from Oxford University Press and Cambridge University Press, and codeveloped the Affective Reactivity Index; **CS** reports non-personal research funds from Lundbeck and Shire paid to his institution; is a consultant and advisory board member of Editorial Médica Panamericana, Medice, NeuroTech Solutions Ltd, and Shire; received speaker's bureau from Medice and Shire, and royalties from Editorial Médica Panamericana, Mayo Ediciones, and Springer SBM Spain; **ES** receives research funding from the UK National Institute of Health Research, United Kingdom Research and Innovation, and the European Innovative Medicines Initiative; **PS** reports grants from Anavex Life Sciences Corp, NIHR Invention for Innovation (i4i) Programme, MRC Clinical Academic Research Partnerships, NIHR HTA, NIHR EME, NIHR PGfAR, British Heart Foundation, Reverse Rett, Newron Pharmaceuticals, HealthTracker, and Anavex Life Sciences Corporation; royalties from HealthTracker; consulting fees from Anavex Life Sciences Corporation; honoraria from the Egyptian Psychiatry Association; and stocks from HealthTracker; **ICKW** received research grants from Amgen, Janssen, GSK, Novartis, Pfizer, Bayer and Bristol-Myers Squibb and Takeda, Institute for Health Research in England, European Commission, National Health and Medical Research Council in Australia, The European Union's Seventh Framework Programme for research, technological development, Research Grants Council Hong Kong and Health and Medical Research Fund Hong Kong; consulting fees from IQVIA and World Health Organization; payment for expert testimony for Appeal Court in Hong Kong; serves on advisory committees for Member of Pharmacy and Poisons Board; is a member of the Expert Committee on Clinical Events Assessment Following COVID-19 Immunization; is a member of the Advisory Panel on COVID-19 Vaccines of the Hong Kong Government; is the non-executive director of Jacobson Medical in Hong Kong; and is the founder and director of Therakind Limited (UK), Advance Data Analytics for Medical Science (ADAMS) Limited (HK), Asia Medicine Regulatory Affairs (AMERA) Services Limited and OCUS Innovation Limited (HK, Ireland and UK). All other authors declare no competing interests.

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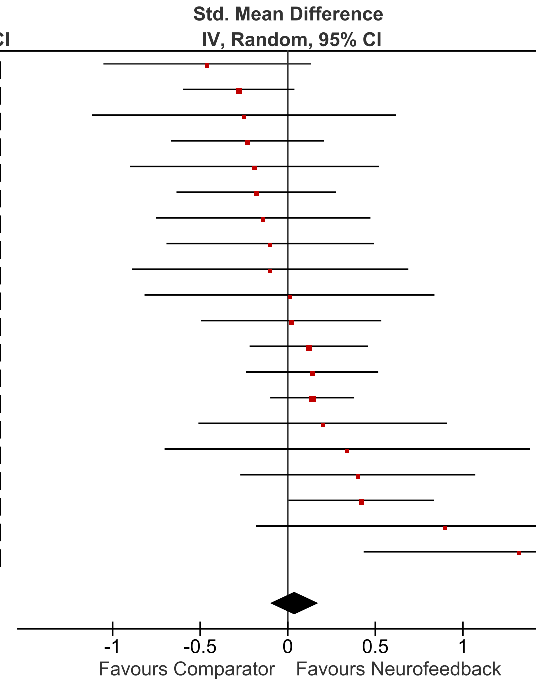
Fig. 1: Forest plots for meta-analysis of effects of PBLIND outcome measures of ADHD total symptoms.

Combined Inattention & Hyperactivity/Impulsivity Symptoms

Study or Subgroup	Std. Mean Difference	SE	Neurofeedback Total	Comparator Total	Weight	Std. Mean Difference IV, Random, 95% CI
Blume et al. (unpublished) - fNIRS 2D	-0.46	0.3	12	11	4.3%	-0.46 [-1.05, 0.13]
Lim et al. (2019)	-0.28	0.16	81	82	9.6%	-0.28 [-0.59, 0.03]
Steiner et al. (2011)	-0.25	0.44	9	13	2.3%	-0.25 [-1.11, 0.61]
Lam et al. (2022)	-0.23	0.22	43	43	6.7%	-0.23 [-0.66, 0.20]
Schönenberg et al. (2017)	-0.18	0.23	37	38	6.3%	-0.18 [-0.63, 0.27]
van Dongen-Boomsma et al. (2013)	-0.14	0.31	22	19	4.1%	-0.14 [-0.75, 0.47]
Blume et al. (unpublished) - fNIRS VR	-0.1	0.3	12	11	4.3%	-0.10 [-0.69, 0.49]
Maurizio et al. (2014)	-0.1	0.4	13	12	2.7%	-0.10 [-0.88, 0.68]
Steiner et al. (2014)	0.01	0.42	34	36	2.5%	0.01 [-0.81, 0.83]
Minder et al. (2018)	0.02	0.26	19	19	5.4%	0.02 [-0.49, 0.53]
Arnold et al. (2013)	-0.19	0.36	25	11	3.2%	-0.19 [-0.90, 0.52]
Strehl et al. (2017)	0.12	0.17	75	69	9.0%	0.12 [-0.21, 0.45]
Korfmacher et al. (2022)	0.14	0.19	55	58	8.0%	0.14 [-0.23, 0.51]
Arnold et al. (2021)	0.14	0.12	84	58	12.1%	0.14 [-0.10, 0.38]
Alegria et al. (2017)	0.2	0.36	18	13	3.2%	0.20 [-0.51, 0.91]
Zilverstand et al. (2017)	0.34	0.53	7	6	1.7%	0.34 [-0.70, 1.38]
Bakhshayesh et al. (2011)	0.4	0.34	18	17	3.6%	0.40 [-0.27, 1.07]
Gevensleben et al. (2009)	0.42	0.21	59	35	7.1%	0.42 [0.01, 0.83]
Baumeister et al. (2018)	0.9	0.55	8	7	1.5%	0.90 [-0.18, 1.98]
Shereena et al. (2019)	1.32	0.45	14	11	2.2%	1.32 [0.44, 2.20]
Total (95% CI)			**645**	**569**	**100.0%**	**0.04 [-0.10, 0.18]**

Heterogeneity: Tau² = 0.03; Chi² = 27.37, df = 19 (P = 0.10); I² = 31%
Test for overall effect: Z = 0.58 (P = 0.56)



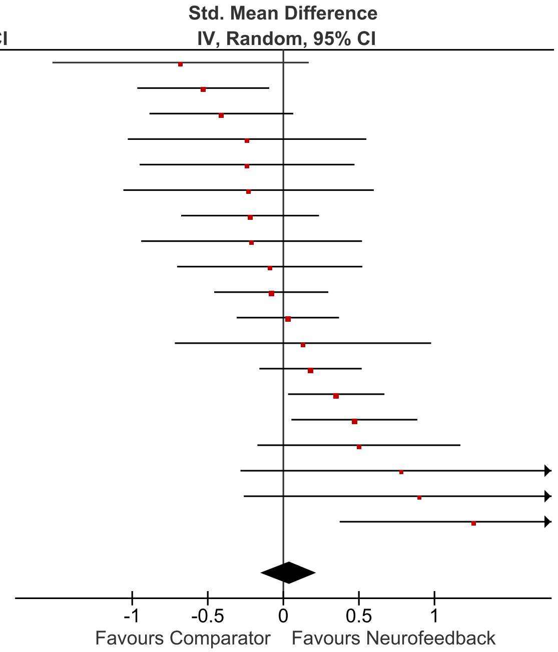
Note. SE Standard Error, Std. Standardised.

Fig. 2: Forest plots for meta-analysis of effects of PBLIND outcome measures of ADHD inattention (upper panel) and hyperactivity/impulsivity (lower panel) symptoms.

Inattention Symptoms

Study or Subgroup	Std. Mean Difference	SE	Neurofeedback Total	Comparator Total	Weight	Std. Mean Difference IV, Random, 95% CI
Blume et al. (unpublished)	-0.68	0.43	12	11	3.4%	-0.68 [-1.52, 0.16]
Lam et al. (2022)	-0.53	0.22	43	43	7.0%	-0.53 [-0.96, -0.10]
Steiner et al. (2014)	-0.41	0.24	34	36	6.5%	-0.41 [-0.88, 0.06]
Maurizio et al. (2014)	-0.24	0.4	13	12	3.7%	-0.24 [-1.02, 0.54]
Arnold et al. (2013)	-0.24	0.36	25	11	4.3%	-0.24 [-0.95, 0.47]
Blume et al. (unpublished)	-0.23	0.42	12	11	3.5%	-0.23 [-1.05, 0.59]
Schönenberg et al. (2017)	-0.22	0.23	37	38	6.8%	-0.22 [-0.67, 0.23]
Alegria et al. (2017)	-0.21	0.37	18	13	4.1%	-0.21 [-0.94, 0.52]
van Dongen-Boomsma et al. (2013)	-0.09	0.31	22	19	5.1%	-0.09 [-0.70, 0.52]
Korfmacher et al. (2022)	-0.08	0.19	55	58	7.7%	-0.08 [-0.45, 0.29]
Strehl et al. (2017)	0.03	0.17	75	69	8.2%	0.03 [-0.30, 0.36]
Steiner et al. (2011)	0.13	0.43	9	13	3.4%	0.13 [-0.71, 0.97]
Arnold et al. (2021) - Conners 3P (T)	0.18	0.17	84	58	8.2%	0.18 [-0.15, 0.51]
Lim et al. (2019)	0.35	0.16	81	82	8.5%	0.35 [0.04, 0.66]
Gevensleben et al. (2009)	0.47	0.21	59	35	7.2%	0.47 [0.06, 0.88]
Bakhshayesh et al. (2011)	0.5	0.34	18	17	4.6%	0.50 [-0.17, 1.17]
Baumeister et al. (2018)	0.78	0.54	8	7	2.4%	0.78 [-0.28, 1.84]
Zilverstand et al. (2017)	0.9	0.59	7	6	2.1%	0.90 [-0.26, 2.06]
Shereena et al. (2019)	1.26	0.45	14	11	3.2%	1.26 [0.38, 2.14]
Total (95% CI)			**626**	**550**	**100.0%**	**0.04 [-0.15, 0.22]**

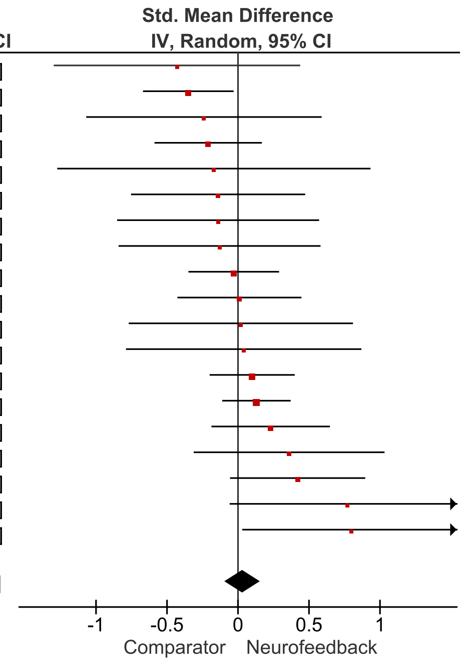
Heterogeneity: Tau² = 0.08; Chi² = 38.70, df = 18 (P = 0.003); I² = 53%
Test for overall effect: Z = 0.40 (P = 0.69)



Hyperactivity/Impulsivity Symptoms

Study or Subgroup	Std. Mean Difference	SE	Neurofeedback Total	Comprator Total	Weight	Std. Mean Difference IV, Random, 95% CI
Steiner et al. (2011)	-0.43	0.44	9	13	1.9%	-0.43 [-1.29, 0.43]
Lim et al. (2019)	-0.35	0.16	81	82	10.3%	-0.35 [-0.66, -0.04]
Blume et al. (unpublished)	-0.24	0.42	12	11	2.1%	-0.24 [-1.06, 0.58]
Korfmacher et al. (2022)	-0.21	0.19	55	58	8.1%	-0.21 [-0.58, 0.16]
Zilverstand et al. (2017)	-0.17	0.56	7	6	1.2%	-0.17 [-1.27, 0.93]
van Dongen-Boomsma et al. (2013)	-0.14	0.31	22	19	3.6%	-0.14 [-0.75, 0.47]
Alegria et al. (2017)	-0.14	0.36	18	13	2.8%	-0.14 [-0.85, 0.57]
Arnold et al. (2013)	-0.13	0.36	25	11	2.8%	-0.13 [-0.84, 0.58]
Schönenberg et al. (2017)	-0.03	0.16	37	38	10.3%	-0.03 [-0.34, 0.28]
Lam et al. (2022)	0.01	0.22	43	43	6.5%	0.01 [-0.42, 0.44]
Maurizio et al. (2014)	0.02	0.4	13	12	2.3%	0.02 [-0.76, 0.80]
Blume et al. (unpublished)	0.04	0.42	12	11	2.1%	0.04 [-0.78, 0.86]
Arnold et al. (2021) - Conners 3P DSM-Hyp/Imp	0.1	0.15	84	58	11.2%	0.10 [-0.19, 0.39]
Strehl et al. (2017)	0.13	0.12	75	69	14.5%	0.13 [-0.11, 0.37]
Gevensleben et al. (2009)	0.23	0.21	59	35	7.0%	0.23 [-0.18, 0.64]
Bakhshayesh et al. (2011)	0.36	0.34	18	17	3.1%	0.36 [-0.31, 1.03]
Steiner et al. (2014)	0.42	0.24	34	36	5.6%	0.42 [-0.05, 0.89]
Shereena et al. (2019)	0.77	0.42	14	11	2.1%	0.77 [-0.05, 1.59]
Baumeister et al. (2018)	0.8	0.39	8	7	2.4%	0.80 [0.04, 1.56]
Total (95% CI)			**626**	**550**	**100.0%**	**0.03 [-0.09, 0.16]**

Heterogeneity: Tau² = 0.01; Chi² = 22.15, df = 18 (P = 0.23); I² = 19%
Test for overall effect: Z = 0.54 (P = 0.59)



Note. SE Standard Error, Std. Standardised.

Table 1. Summary of results showing pooled standardized mean differences (SMD; with Hedges' g adjustment) between treatment and control arms for PBLIND measures of ADHD symptoms at the first assessment after the final neurofeedback session. *Significant values are bolded.*

				Effect Size Estimate				Heterogeneity		
PBLIND Outcome	**RCTs Included**	***k***	***n***	**SMD**	**Lower 95%CI**	**Upper 95%CI**	***p***	***Q***	**I^2**	***P***
ADHD Total	All	20	1214	0.04	-0.10	0.18	0.56	27.37	31	0.10
	EEG only	15	1038	0.09	-0.07	0.25	0.29	21.98	36	0.08
	FBT	9	609	0.02	-0.22	0.27	0.85	**15.82**	**49**	**0.04**
	SCP	4	na	na	na	na	na	na	na	na
	Standard Protocol	9	681	**0.21**	**0.02**	**0.40**	**0.03**	12.96	38	0.11
	Hemodynamic only	5	176	-0.15	-0.42	0.11	0.26	3.03	0	0.55
	Active, non-pharmacological	2	na	na	na	na	na	na	na	na
	Sham, semi-active	14	783	0.05	-0.09	0.20	0.45	14.44	10	0.34
	TAU	2	na	na	na	na	na	na	na	na
	WLC	2	na	na	na	na	na	na	na	na
	With learning	5	238	0.23	-0.03	0.49	0.08	2.20	0	0.70
	Children only	18	1126	0.05	-0.10	0.20	0.50	26.11	35	0.07
	Same intervention and PBLIND setting	2	na	na	na	na	na	na	Na	na
Inattention	All	19	1176	0.04	-0.15	0.22	0.69	**38.71**	**54**	**0.003**
	EEG only	14	1000	0.12	-0.07	0.30	0.23	**24.84**	**48**	**0.02**
	FBT	9	609	0.11	-0.16	0.38	0.41	**18.38**	**57**	**0.02**
	SCP	3	na	na	na	na	na	na	Na	na
	Standard Protocol	8	643	0.22	-0.03	0.47	0.08	**15.40**	**55**	**0.03**
	Hemodynamic only	5	176	-0.29	-0.69	0.11	0.15	5.98	33	0.20
	Active, non-pharmacological	1	na	na	na	na	na	na	Na	na
	Sham, semi-active	14	783	-0.01	-0.21	0.20	0.96	**23.46**	**45**	**0.04**
	TAU	2	na	na	na	na	na	na	na	na
	WLC	2	na	na	na	na	na	na	na	na
	With learning	5	238	0.22	-0.13	0.58	0.21	5.50	27	0.24
	Children only	17	1088	0.04	-0.16	0.23	0.71	**35.26**	**55**	**0.004**
	Same intervention and PBLIND setting	2	na	na	na	na	na	na	Na	na

Hyperactivity/ Impulsivity	All	19	1176	0.03	-0.09	0.16	0.59	22.15	19	0.23
	EEG only	14	1000	0.06	-0.10	0.22	0.45	21.32	39	0.07
	FBT	9	609	0.03	-0.19	0.24	0.80	14.10	43	0.08
	SCP	3	na	na	na	na	na	na	na	na
	Standard Protocol	8	643	0.13	-0.04	0.30	0.14	10.10	31	0.18
	Hemodynamic only	5	176	-0.06	-0.36	0.24	0.70	0.43	0	0.98
	Active, non-pharmacological	1	na	na	na	na	na	na	na	na
	Sham, semi-active	14	783	0.08	-0.04	0.20	0.19	7.39	0	0.88
	TAU	2	na	na	na	na	na	na	na	na
	WLC	2	na	na	na	na	na	na	na	na
	With learning	5	238	0.17	-0.05	0.39	0.12	4.14	3	0.39
	Children only	17	1088	0.05	-0.09	0.19	0.51	21.84	27	0.15
	Same intervention and PBLIND setting	2	na	na	na	na	na	na	na	na

Legend. EEG, electroencephalogram; FBT, Frequency Band Training; SCP, Slow Cortical Potentials; TAU, Treatment-As-Usual; WLC, Waitlist-Control.

Table 2. Summary of results showing pooled standardized mean differences (SMD; with Hedges' g adjustment) between treatment and control arms for neuropsychological measures at the first assessment after the final neurofeedback session. Significant values are bolded.

				Effect Size Estimate				Heterogeneity		
Outcome	**RCTs Included**	***k***	***n***	**SMD**	**Lower 95%CI**	**Upper 95%CI**	***p***	**Q**	**I²**	***p***
Attention	All	25	1140	0.04	-0.19	0.26	0.75	**76**	**68**	**<.001**
	EEG only	19	922	0.11	-0.15	0.37	0.40	**64**	**72**	**<.001**
	FBT	11	444	0.38	-0.05	0.81	0.08	**45**	**78**	**<.001**
	SCP	5	260	-0.27	-0.63	0.08	0.13	7	42	0.14
	Standard Protocol	15	687	0.18	-0.16	0.52	0.29	**61**	**77**	**<.001**
	Hemodynamic only	6	218	-0.21	-0.63	0.20	0.31	10	51	0.07
	Active, non-pharmacological	3	na	na	na	na	na	na	na	na
	Sham, semi-active	16	687	0.06	-0.30	0.41	0.76	**72**	**79**	**<.001**
	TAU	4	na	na	na	na	na	na	na	na
	WLC	2	na	na	na	na	na	na	na	na
	With learning	7	247	0.35	-0.55	1.25	0.45	**58**	**90**	**<.001**
	Children only	22	1040	0.03	-0.22	0.28	0.81	**75**	**72**	**<.001**
Inhibition	All	21	990	0.08	-0.10	0.26	0.39	**48**	**59**	**<.001**
	EEG only	15	778	0.04	-0.16	0.24	0.72	**26**	**45**	**0.03**
	FBT	8	335	0.22	-0.12	0.56	0.20	**16**	**56**	**0.03**
	SCP	5	260	-0.07	-0.35	0.20	0.61	5	14	0.32
	Standard Protocol	13	610	0.06	-0.18	0.31	0.61	**25**	**52**	**0.01**
	Hemodynamic only	6	212	0.20	-0.23	0.64	0.36	**21**	**76**	**0.001**
	Active, non-pharmacological	3	na	na	na	na	na	na	na	na
	Sham, semi-active	12	538	0.05	-0.21	0.31	0.69	**32**	**66**	**0.001**
	TAU	4								
	WLC	2	na	na	na	na	na	na	na	na
	With learning	5	171	0.41	-0.14	0.96	0.14	**22**	**81**	**<.001**
	Children only	18	890	0.12	-0.11	0.35	0.29	**43**	**61**	**<.001**
Verbal WM	All	9	455	-0.04	-0.19	0.11	0.58	4	0	0.85
	EEG only	7	401	-0.05	-0.21	0.11	0.53	4	0	0.69

	FBT	4	na	na	na	na	na	na	na	na
	SCP	2	na	na	na	na	na	na	na	na
	Standard Protocol	4	na	na	na	na	na	na	na	na
	Hemodynamic only	2	na	na	na	na	na	na	na	na
	Active, non-pharmacological	0	na	na	na	na	na	na	na	na
	Sham, semi-active	4	na	na	na	na	na	na	na	na
	TAU	3	na	na	na	na	na	na	na	na
	WLC	2	na	na	na	na	na	na	na	na
	With learning	1	na	na	na	na	na	na	na	na
	Children only	6	357	-0.14	-0.39	0.12	0.30	8	35	0.17
Visual WM	All	7	449	-0.10	-0.24	0.04	0.17	3	0	0.79
	EEG only	7	349	-0.10	-0.25	0.06	0.21	3	0	0.64
	FBT	3	na	na	na	na	na	na	na	na
	SCP	1	na	na	na	na	na	na	na	na
	Standard Protocol	3	na	na	na	na	na	na	na	na
	Hemodynamic only	2	na	na	na	na	na	na	na	na
	Active, non-pharmacological	0	na	na	na	na	na	na	na	na
	Sham, semi-active	4	na	na	na	na	na	na	na	na
	TAU	3	na	na	na	na	na	na	na	na
	WLC	0	na	na	na	na	na	na	na	na
	With learning	1	na	na	na	na	na	na	na	na
	Children only	6	436	-0.11	-0.25	0.04	0.14	3	0	0.75
Processing Speed	All	15	909	**0.35**	**0.01**	**0.69**	**0.04**	**85**	**84**	**<.001**
	EEG only	13	909	**0.35**	**0.01**	**0.69**	**0.04**	**85**	**84**	**<.001**
	FBT	8	365	0.67	-0.06	1.39	0.07	**72**	**90**	**<.001**
	SCP	3	909	**0.35**	**0.01**	**0.69**	**0.04**	**85**	**84**	**<.001**
	Standard Protocol	11	641	**0.48**	**0.00**	**0.95**	**0.05**	**80**	**87**	**<.001**
	Hemodynamic only	2	na	na	na	na	na	na	na	na
	Active, non-pharmacological	2	na	na	na	na	na	na	na	na
	Sham, semi-active	11	**632**	**0.57**	**0.11**	**1.02**	**0.01**	73	86	**<.001**
	TAU	2	na	na	na	na	na	na	na	na

	WLC	2	na	na	na	na	na	na	na	na
	With learning	4	na	na	na	na	na	na	na	na
	Children only	12	747	0.34	-0.07	0.75	0.11	79	86	**<.001**
BRIEF - GEC	All	7	385	0.13	-0.04	0.30	0.13	3	0	0.81
	EEG only	7	385	0.13	-0.04	0.30	0.13	3	0	0.81
	FBT	3	na	na	na	na	na	na	na	na
	SCP	2	na	na	na	na	na	na	na	na
	Standard Protocol	2	na	na	na	na	na	na	na	na
	Hemodynamic only	0	na	na	na	na	na	na	na	na
	Active, non-pharmacological	1	na	na	na	na	na	na	na	na
	Sham, semi-active	2	na	na	na	na	na	na	na	na
	TAU	3	324	0.14	-0.04	0.33	0.13	3	0	0.60
	WLC	1	324	0.14	-0.04	0.33	0.13	3	0	0.60
	With learning	0	na	na	na	na	na	na	na	na
	Children only	7	385	0.13	-0.04	0.30	0.13	3	0	0.81

Legend. BRIEF, Behavior Rating Inventory of Executive Function; EEG, electroencephalogram; FBT, Frequency Band Training; GEC, Global Executive Composite; SCP, Slow Cortical Potentials; TAU, Treatment-As-Usual; WLC, Waitlist-Control; WM, working memory