Research in Developmental Disabilities 118 (2021) 104063

Contents lists available at ScienceDirect

Research in Developmental Disabilities

journal homepage: www.elsevier.com/locate/redevdis

The relationship between internalizing problems and acute exercise duration in children with attention-deficit/hyperactivity disorder: The role of frontal alpha asymmetry

Ting-Yu Chueh [a], Shu-Shih Hsieh [b,c], Yu-Jung Tsai [a], Chien-Lin Yu [a], Chung-Ju Huang [d], Tsung-Min Hung [a,e,*]

[a] *Department of Physical Education and Sport Sciences, National Taiwan Normal University, Taipei, Taiwan*
[b] *Department of Psychology, Northeastern University, Boston, United States*
[c] *Department of Psychology, Kingston University, Kingston upon Thames, United Kingdom*
[d] *Graduate Institute of Sport Pedagogy, University of Taipei, Taipei, Taiwan*
[e] *Institute for Research Excellence in Learning Science, National Taiwan Normal University, Taipei, Taiwan*

ARTICLE INFO

No. of reviews completed is 3

Keywords:
Approach/withdrawal model
Acute exercise
Dose-response
EEG

ABSTRACT

Background: Frontal alpha asymmetry (FAA) has been associated with the regulation of certain types of internalizing psychopathologies, and is affected by acute aerobic exercise (AE). However, no previous studies have examined the association between FAA and internalizing problems or the effects of acute exercise on FAA in children with ADHD.
Aims: This study had two objectives. First, it aimed to examine the relationship between FAA and internalizing behaviors in children with ADHD. Second, it sought to investigate the differential effects of acute AE (30 and 50 min) on FAA.
Method: Participants were assigned to one of the following three groups: 50 min of AE, 30 min of AE, and a control group. Resting electroencephalogram (EEG) data were recorded before and after their respective treatments. EEG data from 43 participants were analyzed to investigate the association between pre-test FAA and internalizing problems as assessed by Child Behavior Checklist scores. Additionally, EEG data from 46 participants were analyzed to examine the effects of acute AE on post-test FAA while controlling for pre-test FAA.
Results: Pre-test FAA was found to be significantly negatively associated with internalizing problems, with both hemispheres contributing to this association. Regarding the effects of acute exercise, the 50-minute AE group had highest post-test FAA, reflected by the increased relative left-side frontal activity.
Conclusions: These findings suggest that FAA is a biological marker of internalizing symptoms in children with ADHD, and a 50-minute session of AE can effectively modulate FAA.

Highlights

✓ Lower frontal alpha asymmetry (characterized by relatively lower left-side frontal activity and greater right-side frontal activity) is associated with internalizing problems in children with attention-deficit/hyperactivity disorder, with both hemispheres contributing to this relationship.

* Corresponding author. E-mail address: ernesthungkimo@yahoo.com.tw (T.-M. Hung).

https://doi.org/10.1016/j.ridd.2021.104063
Received 25 September 2020; Received in revised form 30 July 2021; Accepted 10 August 2021
Available online 7 September 2021

✓ Fifty minutes of acute moderate-intensity aerobic exercise can increase frontal alpha asymmetry, predominately resulting from increased left-side frontal activity (lower alpha power), in children with attention-deficit/hyperactivity disorder.

1. Introduction

Attention-deficit/hyperactivity disorder (ADHD) is one of the most common psychiatric disorders in children, affecting 7.2 % of school-aged children globally (Thomas, Sanders, Doust, Beller, & Glasziou, 2015). Children with ADHD have elevated levels of anxiety and depression (Jerrell, McIntyre, & Park, 2015; Leirbakk, Clench-Aas, & Raanaas, 2015; Shea, Lee, Lai, Luk, & Leung, 2018), which are frequently accompanied with somatic complaints such as headache, abdominal pain, fatigue, and back pain (Leirbakk et al., 2015). These negative emotional symptoms are referred to as internalizing problems and are manifested in daily behaviors (Achenbach & Rescorla, 2001). Internalizing problems have been implicated in social competence (Blackman, Ostrander, & Herman, 2005; Mikami, Ransone, & Calhoun, 2011), daily functioning (Sciberras et al., 2014), and self-injury behavior risk (Kang et al., 2019; Lin, You, Wu, & Jiang, 2018). Internalizing problems may result from dysfunctional dopaminergic and serotonergic systems that play important roles in the regulation of emotion and motivation (Canli & Lesch, 2007; Salgado-Pineda, Delaveau, Blin, & Nieoullon, 2005). Fortunately, these neurotransmitter systems can be enhanced by repetitively acute bouts of exercise (for review, see Wegner et al., 2014), which have been found to increase monoamine levels (for review, see Basso & Suzuki, 2017). Frontal alpha asymmetry (FAA), which is measured by electroencephalogram (EEG), is associated with monoamine neurotransmitter systems (Mann et al., 1996; Wacker, Mueller, Pizzagalli, Hennig, & Stemmler, 2013) and used to study regulation of emotion and motivation (Harmon-Jones & Gable, 2017; Reznik & Allen, 2018). A recent review reported that acute bouts of aerobic exercise (AE) improved FAA and emotional regulation in healthy young adults (Silveira et al., 2019). Accordingly, to support the design of evidence-based interventions to alleviate internalizing problems in children with ADHD, this study first identified whether FAA can be used as a biomarker of internalizing problems and then examined the effects of different durations of acute AE on FAA in children with ADHD.

1.1. FAA and internalizing problems

The approach/withdrawal motivational model of FAA postulates that left-side frontal areas are primarily associated with approach motivation, whereas right-side frontal areas are associated with withdrawal motivation (for review, see Harmon-Jones & Gable, 2017; Reznik & Allen, 2018). FAA is a relative measure of the difference in EEG alpha power between homologous right and left frontal electrodes (e.g., right minus left frontal alpha). Studies combining EEG with hemodynamic measures have shown that alpha power is inversely related to cortical activity (Laufs et al., 2003; Oakes et al., 2004). As such, decreased FAA could reflect either relatively lower left-side frontal activity or relatively greater right-side frontal activity, and the reverse is true for increased FAA. Lower FAA is thus associated with more withdrawal or less approach motivation and might influence an individual's vulnerability to developing internalizing symptoms. A substantial number of studies have reported a link between lower FAA in resting state and internalizing symptoms forms of psychopathology (Feldmann et al., 2018; Kemp et al., 2010; Stewart, Bismark, Towers, Coan, & Allen, 2010; Stewart, Coan, Towers, & Allen, 2014). Additionally, studies have found that neurofeedback training, with the aim of increasing FAA, resulted in reduced internalizing problems (Harmon-Jones, Harmon-Jones, Fearn, Sigelman, & Johnson, 2008; Mennella, Patron, & Palomba, 2017; Peeters, Ronner, Bodar, van Os, & Lousberg, 2014). Although these results suggest that FAA could be a biomarker of internalizing problems, the association between internalizing problems and FAA in children with ADHD was unknown. Thus, the first aim of the current study was to fill this research gap.

1.2. Acute aerobic exercise and FAA

Although previous studies reported no positive effects of acute bouts of 20–30-minute moderate-intensity AE on FAA in adults (Lattari et al., 2016; Petruzzello & Tate, 1997), several studies have reported that 30 min of acute moderate-intensity AE positively affected FAA in healthy young adults (Hicks, Hall, Staines, & McIlroy, 2018; Ohmatsu et al., 2014; Woo, Kim, Kim, Petruzzello, & Hatfield, 2009). Moreover, Woo et al. (2009) found that a 30-minute bout of moderate-intensity AE resulted in higher FAA as well improved affect when compared to 45-minute AE, 15-minute AE, or no-exercise condition in healthy young adults. It was reported that this effect was primarily due to altered left-side frontal activity. However, Herring, Monroe, Gordon, Hallgren, and Campbell (2019)) found that a 35–40-minute bout of moderate-to-vigorous-intensity AE led to improved affect in individuals with anxiety disorders. Similar results were seen with 40–60 min of moderate-intensity exercise (Brand et al., 2018). Given that post-exercise FAA has been reported as being related to the concurrent positive affective state (Petruzzello, Hall, & Ekkekakis, 2001; Woo et al., 2009, 2010), longer periods of AE might be beneficial to FAA in individuals with high levels of internalizing symptoms.

Individuals with internalizing disorders and children with ADHD have both been implicated in dysfunction of the dopaminergic and serotonergic systems (Canli & Lesch, 2007; Paclt et al., 2005; Salgado-Pineda et al., 2005; Volkow et al., 2011), which may modulate the effect of acute bouts of AE on FAA. Previous studies have shown that these two neuromodulators might, at least partly, explain the mechanism by which acute bouts of AE alter FAA. AE is known to increase dopamine and serotonin levels (for review, see Basso & Suzuki, 2017). Ohmatsu et al. (2014) reported that the improvements seen in FAA following acute bouts of AE were positively correlated with increases in serotonin levels. With respect to potential dopaminergic effects, findings from Wacker (2018) support a dopaminergic basis for frontal EEG asymmetry. However, the downstream effects of these two neurochemical factors on the frontal lobe, such as regulation of motivation and emotion (Canli & Lesch, 2007; Salgado-Pineda et al., 2005), might depend on the density of serotonergic/dopaminergic terminals and receptors (Celada, Puig, & Artigas, 2013; Schultz, Tremblay, & Hollerman, 1998). Children with ADHD exhibited less dopaminergic response to 30-minute bouts of AE compared to healthy controls, suggesting an impaired dopaminergic system (Wigal et al., 2003). Thus, while a previous study has suggested that a 30-minute bout of AE was optimal for FAA modulation in young adults (Woo et al., 2009), for children with ADHD, relatively longer periods of AE may be required to offset their impaired monoaminergic systems.

1.3. Aims

To provide practical implications for treating internalizing syndromes in children with ADHD, this study aimed to 1) investigate the association between internalizing problems and FAA and, 2) examine the effects of different durations (30 and 50 min) of acute moderate-intensity AE on FAA. We hypothesized that FAA would be negatively correlated with internalizing problems in children with ADHD Regarding the effects of acute exercise, we hypothesized that children with ADHD would exhibit the highest FAA after 50 min of exercise relative to the control group, with left-side frontal alpha power correlating with this effect.

2. Method

2.1. Participants

A total of 56 children with ADHD (5 girls), aged 7–12 years, were recruited from elementary schools in [BLINDED FOR REVIEW]. All participants met the following inclusion criteria: (1) diagnosed by a medical professional as having ADHD based on the revised procedures of the fourth edition of the Diagnostic and Statistical Manual for Mental Disorders (DSM-IV-TR); (2) no history of brain injury or neurological conditions such as epileptic seizures, serious head injuries, or periods of unconsciousness; (3) free of intellectual disability. Furthermore, participants were excluded from analysis the study if they: (1) had an intellectual development disorder (nonverbal intelligence quotient [IQ] test scores < 75); (2) demonstrated motor impairment (Movement Assessment Battery for Children [MABC2] scores < 5); or (3) produced poor EEG data (i.e., 50 % epochs rejected) in either open or closed eye conditions, which is the minimum duration (i.e., 2 min) required for spectral analysis (Nuwer et al., 1999; Pivik et al., 1993).

2.2. Design and procedure

Participants were randomly assigned to one of the following three groups: (1) a 50-minute exercise group (50 EG, n = 18); (2) a 30-minute exercise group (30 EG, n = 19); or (3) a control group (CG, n = 19, 30 min of video watching). After randomization, six participants voluntarily withdrew from the experiment due to motivational reasons (3 from the 50 EG and 3 from the CG). Thus, 50 participants successfully completed the study. A previous study reported that the effect size of differences in FAA between individuals with internalizing problem disorders and healthy controls was 0.93 (Cohen's *d*) (Stewart et al., 2010). This effect size was converted to a correlation coefficient (0.422) based on the formula: $r = d/\sqrt{4 + d^2}$. Power analysis was then used to determine the adequate sample

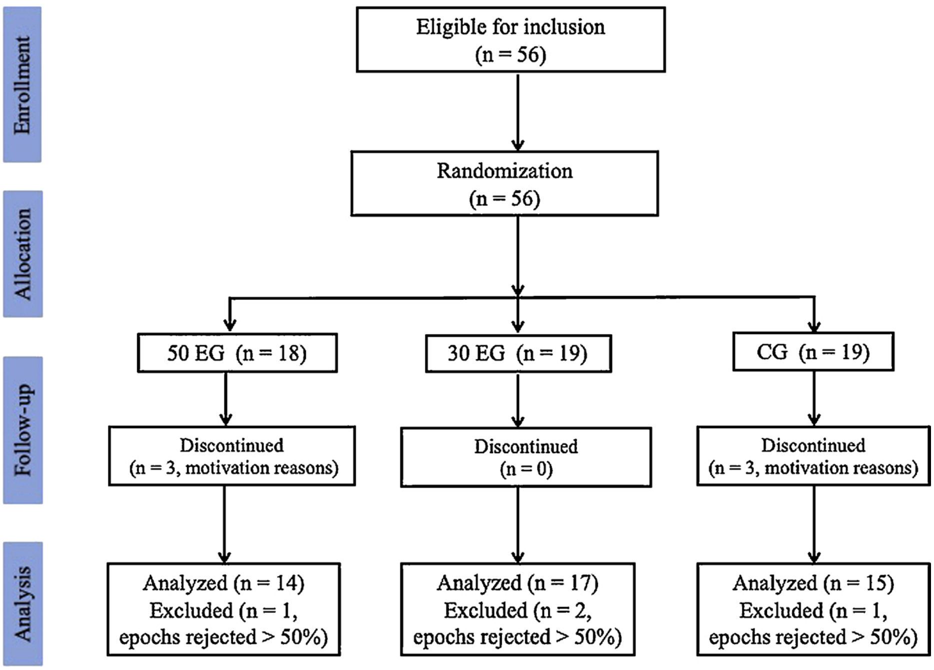

Fig. 1. A flow diagram of the study.

size for correlation analysis. The results showed that 42 participants were sufficient to achieve a power of 0.8, assuming alpha = 0.05, according to the formula from Hulley, Cummings, Browner, Grady, and Newman (2013) (see **supplementary document 1**). This sample size is also sufficient when examining the effects of acute moderate-intensity AE on FAA based on effect sizes (η^2_p = 0.2 to 0.39) from previous studies (Hicks et al., 2018; Woo, Kim, Kim, Petruzzello, & Hatfield, 2010) in power analysis (power = 0.8, alpha = 0.05) (Faul, Erdfelder, Buchner, & Lang, 2009). Thus, the reduced sample size was still adequate to detect expected results. Fig. 1 is a flow diagram showing the enrollment procedure.

The participants visited the laboratory on two separate days at an interval 7–14 days. They were required to refrain from food and drink consumption, except water, for 1.5 h prior to testing, and refrain from all medications or engagement in behavioral treatments for at least 24 h prior to each session. On day 1, the experimental procedure was explained to the participants and their legal guardians, and the latter were asked to complete an informed consent form based on the protocols approved by [BLINDED FOR REVIEW]. The legal guardians were then asked to provide their child's health history and complete a descriptive questionnaire and a Chinese version of the CBCL (Chen, Huang, & Chao, 2006). Thereafter, a nonverbal IQ test (TONI-2) (Brown, Sherbenou, & Johnsen, 1990) and the second edition of the MABC2 (Henderson, Sugden, & Barnett, 2007) were administered to the participants to assess intellectual development disorders and motor impairments, respectively.

On day 2, the participants were instructed to sit on a chair in a sound-attenuated testing room where they were fitted with a 32-electrode cap, and EEG recordings were taken. After two researchers verified that the impedance of the EEG signal was below 5 kΩ, the participants were instructed to sit calmly and resting EEG measures were taken. These resting measurements consisted of four 1-minute trials, a duration which has been shown to provide a reliable baseline measure of FAA (Hagemann, 2004; Smith, Reznik, Stewart, & Allen, 2017). Two of the trials required the children to sit with their eyes open (O) gazing at a cross on the screen, and two trials were conducted with their eyes closed (C). A 30-second break was taken between each trial. During the resting EEG data collection, the resting heart rate (HR) was also assessed using an HR monitor (Polar RS800CX; Polar Electro Oy, Kempele, Finland). The participants were then randomly assigned to one of the three experimental groups: 50 EG, 30 EG, and CG. After completing their assigned treatments, the same procedures as those for the pre-test EEGs were performed to determine the post-test EEGs. To allow time for the HR to return to within 10 % of the baseline HR level after the exercise intervention (Pontifex, Saliba, Raine, Picchietti, & Hillman, 2013), post-EEG recordings were taken approximately 15 min after each treatment for all three groups. During the recovery period, EEG impedance was verified.

2.3. Measurement

2.3.1. Descriptive variables

Sex, age, health history, and current medication use were reported by the legal guardians. The participants' handedness was orally reported by their legal guardian and then verified using motor competence assessments (MABC2) consisting of several manual dexterity tasks such as drawing and throwing (Henderson et al., 2007). IQ was assessed using the Test of Nonverbal Intelligence, Second Edition (Brown et al., 1990).

2.3.2. Chinese version of the child behavior checklist

The Chinese version of the CBCL (Chen et al., 2006) is based on the Achenbach System of Empirically Based Assessment (Achenbach & Rescorla, 2001), which uses parental ratings of their children to yield three broad syndrome scales: internalizing problems (anxious/depressed, withdrawn/depressed, and somatic complaints), externalizing problems (rule-breaking and aggressive behaviors), and combined problems (social, thought, and attention problems). A total problem score is obtained by summing the three subscale scores. Although our main interest was to examine FAA and internalizing symptoms, we also included externalizing symptoms to examine whether our findings were specific to internalizing symptoms. The raw scores were converted into age- and sex-adjusted T-scores based on nationwide normative data (Chen et al., 2006). For the internalizing and externalizing problem subscales, Cronbach's alpha coefficients have been reported as 0.90 and 0.94, respectively, and the mean test-retest reliability coefficients have been reported as 0.91 and 0.92, respectively (Albores-Gallo et al., 2007).

2.3.3. Motor competence assessments

Motor competence was measured by the MABC2 (Henderson et al., 2007), which is composed of eight fine and gross motor subtests categorized into three domains: manual dexterity (placing pegs, threading lace, and drawing trials), ball skills (two-handed catch and throwing a beanbag onto a mat), and static and dynamic balance (one-board balance, walking heel-to-toe forward, and hopping on mats). A total age-adjusted standard score below 5 indicates the presence of a motor impairment. The test-retest reliability for the total score has been reported as 0.97 (Wuang, Su, & Su, 2012).

2.3.4. Electrophysiological recording and analyzing

EEG activity was recorded at 32 sites using an elastic electrode cap (Quick-Cap; Compumedics Neuroscan, Inc., Charlotte, NC, USA). The electrode sites were mounted according to the modified International 10–20 System. Continuous EEG recordings were taken with linked mastoids as the reference, and the FPz site was used as the ground electrode. Additionally, vertical and horizontal electrooculograms (VEOG and HEOG, respectively) were collected in bipolar configurations located superior and inferior to the right eye and on the left and right orbital canthi. All EEG data were recorded and stored using NeuroScan NuAmps acquisition amplifiers (NeuroScan, Charlotte, NC, USA) with the high-pass filter at DC, and a low-pass filter at 100 Hz. A notch filter of 60 Hz was applied during the data acquisition. EEG data were analyzed using EEGLAB (Delorme & Makeig, 2004) software in MATLAB. During data processing, the EEG data were band-pass filtered (1–30 Hz, -6 dB/octave), using the *pop_eegfiltnew* function. Independent component analysis (ICA) decompositions were performed using an extension of the infomax algorithm (Bell & Sejnowski, 1995) estimation to extract sub-Gaussian components using the default settings in EEGLAB (Delorme & Makeig, 2004). The icablinkmetrics function (version 3.1) was then applied to remove eyeblink-related ICA components. Eyeblinks were identified in the input artifact channel (VEOG) by cross-correlating ($p \leq 0.001$) a canonical eyeblink waveform using the eyeblinklatencies function (Pontifex, Miskovic, & Laszlo, 2017). EEG data were then reconstructed without the eyeblink artifacts. The average numbers of eyeblink-related components removed during this process were 0.88 (± 0.66 SD) in the pre-test and 0.86 (± 0.49 SD) in the post-test data sets. Subsequently, continuous EEG data were segmented into 2-second epochs. Epochs with amplitudes outside the range of ±100 μV and clear eye movements by visually inspected were excluded. The mean numbers of rejected epochs were 7.31 (SD = 9.06) in the pre-test and 9.5 (SD = 8.86) in the post-test data sets. Studies have indicated that current source density (CSD)-transformed FAA is a robust measure used to differentiate between individuals with and without internalizing symptoms (Stewart et al., 2010, 2014). As such, we included CSD transformation when quantifying FAA. CSD transformations compute the second spatial derivative of voltage between nearby electrode sites, and use an estimate of sources and sinks on the scalp to increase the contribution of local electrical activities and reduce the effect of distal volume-conducted sources (Carvalhaes & de Barros, 2015; Smith et al., 2017). EEG data were transformed using a spherical spline surface Laplacian algorithm (Perrin, Pernier, Bertrand, & Echallier, 1989) via the CSD toolbox function (Kayser & Tenke, 2006) (smoothing constant lambda = 10^{-5}; spherical spline order = 4). Finally, artifact-free epochs were fast Fourier transformed with a Hamming window to provide computation of spectral power for each frequency band within each 0.5-Hz bin. The alpha band was extracted from data in the 7.5–12.5-Hz range based on a previous study (Hong et al., 2020). As CSD transforming data change the unit of measurement from μV to $\mu V/cm^2$ (10-cm head radius) (Kayser & Tenke, 2006), the unit of the CSD-transformed alpha power was $\mu V^2/cm^2$. The alpha power data[1] was then natural log transformed (ln) as it violated the Shapiro-Wilk normality test ($p < .05$). The FAA score was calculated as the natural log of the right minus left hemispheres (i.e., ln[F4] − ln[F3]) in both the eyes-open and eyes-closed conditions. Other alpha asymmetry indices were calculated using identical estimation procedures to those used for FAA determination to determine the regional specificity of FAA. These were then used to assess lateral FAA (LFAA) (i.e., ln[F8] − ln[F7])[2], central alpha asymmetry (CAA) (i.e., ln[C4] − ln[C3]), and parietal alpha asymmetry (PAA) (i.e., ln[P4] − ln[P3]. It has been argued that the average of eyes-open (O) and eyes-closed (C) conditions provides a more reliable estimate of EEG power and asymmetry than either condition alone (Tomarken, Davidson, Wheeler, & Kinney, 1992). Thus, alpha asymmetry indices of the eyes-closed and eyes-open conditions from each homologous pairs of electrodes (i.e., FAA, LFAA, CAA, and PAA) were averaged.

2.3.5. Treatment protocol

The participants were equipped with a Neuroscan Quickcap during their assigned treatments. The exercise conditions replicated those used by (Chang, Liu, Yu, & Lee, 2012). All exercise interventions were conducted on a treadmill and comprised a 5-minute warm-up, 20 or 40 min of moderate-intensity AE, and a 5-minute cool-down period. Moderate exercise intensity is defined according to the American College of Sports Medicine (2010) guidelines as [(HRmax − Resting HR) × 50–70 % + Resting HR]. HRmax is calculated with the formula 206.9 − (0.67 × age). To ensure that the participants maintained their targeted HR reserve during exercise, they were equipped with an HR-monitoring watch (Polar RS800CX; Polar Electro Oy, Kempele, Finland) and had their HR tracked every 30 s during the exercise period. Additionally, the age-appropriate (OMNI 10-point version) Rating of Perceived Exertion (RPE) scale (Utter, Robertson, Nieman, & Kang, 2002) was used to assess perceived exercise intensity every 2 min during exercise. To minimize confounding effects due to social interactions between the participants and researchers during exercise, the RPE assessment procedure was explained to all participants prior to the exercise treatments. During the exercise treatments, the participants verbally indicated their level of perceived exercise intensity when they were presented with a copy of the RPE scale. In the CG, the participants watched a documentary film about exercise for 30 min while sitting alone in a room. Their mean HR was similarly assessed during this period.

2.4. Statistical analysis

Means and standard errors (SE) were calculated for all descriptive data. Data normality was determined by assessment of skewness and kurtosis, with normal criteria set as ±2 and ±7, respectively (Kline, 2015; Marshall & Mardia, 1985).

2.4.1. Association between asymmetry indices and behavior problems

To assess the association of asymmetry indices with behavioral problems, we assessed the pre-test EEG data. Bivariate correlations using Pearson product-moment coefficients were first conducted between age, socioeconomic status (SES), IQ, motor competence, internalizing problems T-scores (In-T), externalizing problems T-scores (Ex-T), and each asymmetry index. We then investigated which hemisphere contributed to the associations seen between FAA and In-T. We used a hierarchical regression model to test hemisphere specificity. Whole-head alpha power was entered first. Then, the alpha power from the homologous pairs of electrodes (i.e., F4-F3, F8-F7, C4-C3, or P4-P3) when their alpha asymmetry metrics significantly correlating with In-T were concurrently entered. The model was statistically adjusted for the effect of whole-head power in predicting In-T scores to identify the specific hemisphere that drives the

[1] The distribution of CSD power is largely comparable to mastoid reference power.

[2] As the F8 and F7 were at the edge of EEG-recording sites, the precision of estimations by CSD transformation was compromised. Thus, we computed LFAA without CSD transformation.

association between FAA and In-T scores (Allen, Coan, & Nazarian, 2004).

2.4.2. Effect of acute exercise duration on FAA

Prior to examining effects of acute exercise on FAA, a one-way analysis of variance (ANOVA) was performed for each of the three experimental groups to identify any significant differences in height, weight, IQ, SES, In-T, Ex-T, MC, or pre-test FAA, to ensure homogeneity across groups. A one-way ANOVA was then performed to compare average HR during treatment among the three groups. An analysis of covariance (ANCOVA) was then performed to compare the differences in post-test FAA among the groups using the pre-test FAA as the covariate. To specifically investigate which hemisphere contributed to the exercise effect, separate ANCOVAs comparing post-test F3 or F4 alpha power across the groups were performed while controlling for pre-test frontal hemisphere values. Finally, ANCOVAs were performed to investigate the effect of exercise on LFAA, CAA, and PAA across the groups. Post-hoc comparisons were conducted using the least significant difference (LSD) test. Partial eta-squared effect sizes (η^2_p) were reported for significant effects. Data were analyzed using IBM SPSS Statistics 26 with a family-wise alpha threshold for all tests set at $p = 0.05$.

3. Results

3.1. Analyses of descriptive data

Of the original 50 participants who completed the study, four were excluded from the analyses due to poor quality EEG data (i.e., ≥ 50 % epochs rejected) in the pre-test and post-test sections. The remaining participants consisted of 45 males and 1 female, with 25 of the participants taking a low dosage of methylphenidate (Ritalin < 10 mg, Concerta 1⁄4 18 mg). None of the participants were classified as having a motor impairment or an intellectual development disorder. The SES was determined using Hollingshead's two-factor index, which was computed based on the following formula: (occupation score × 7) + (education score × 4). Five levels of SES were defined according to Index of Social Position (ISP) scores: 11–18, 19–29, 30–40, 41–51, and 52–55 (Hollingshead, 1957). Lower ISP scores correspond to higher SES. Age- and sex-adjusted T-scores > 60 were defined as the clinical cut-off for classification of both internalizing and externalizing problems. Due to missing CBCL data for three participants, 43 participants were included in the analyses used to address our first research question. Characteristics of the participants are presented in Table 1.

3.2. Association between asymmetry indices and behavior problems

Table 2 summarizes the results of the initial Pearson product–moment correlations. Regarding the association of asymmetry indices with behavior problems, FAA was negatively associated with In-T ($r = -.437$, $p = .003$), but not Ex-T ($r = -.214$, $p = .169$). As to which hemisphere contributed to the association between FAA and In-T, a hierarchical regression model showed that In-T was negatively correlated with F4 alpha power ($r = -.452$, $p = .003$) and positively correlated with F3 alpha power ($r = .396$, $p = .01$) after controlling for the variance of whole-head alpha power. More detailed information on the hierarchical regression analysis can be found in **supplementary document 2**.

3.3. Effect of acute exercise on FAA

As shown in Table 3, no significant differences ($p > .05$ for all) were observed in any of the descriptive variables across groups, and no significant differences were identified in pre-test FAA among groups ($F(2,43) = .266$, $p = .768$, $\eta^2_p = .012$). As for the exercise manipulation, both exercise groups had higher mean HRs during treatment compared to the control group (50 EG = 148.5 ± 3.0; 30 EG = 152 ± 2.5; CG = 80.9 ± 2.5; $p < .001$ for all), and no significant differences were seen in the mean HR between the two exercise groups ($p = .381$). There was a significant difference in post-test FAA ($F(2,42) = 3.656$, $p = .034$, $\eta^2_p = .148$), with the 50 EG participants having a higher FAA relative to the 30 EG and CG participants, after adjusting for baseline values, with no significant differences seen between the latter groups. In terms of the frontal hemispheres, the 50 EG participants had lower F3 alpha activity (greater left-side frontal activity) compared to the CG participants ($F(2,42) = 6.725$, $p = .003$, $\eta^2_p = .243$), while both the 50 EG and 30 EG participants had lower F4 alpha activity than the CG participants (greater right-side frontal activity ($F(2,42) = 3.733$, $p = .032$, η^2_p

Table 1
Demographic characteristics of the participants (n = 43).

Variable	Mean (SE)
Age (years)	10.0 (0.3)
SES (ISP scores)	28.2 (1.2)
IQ	102.8 (2.3)
MC (standard scores)	11.2 (1.6)
In-T[#]	62.3 (1.5)
Ex-T[#]	67.0 (1.3)

Note: IQ = Intelligence quotient; SES = socioeconomic status; ISP = Index of Social Position; MC = motor competence; In-T = internalizing problems adjusted T-scores; Ex-T = externalizing problems adjusted T-scores.

Table 2
Bivariate correlation results (n = 43).

Variable	IQ	SES	MC	In-T	Ex-T	FAA	LFAA	CAA	PAA
Age	−.281	.128	.007	−.339*	−.369*	.357*	.032	.146	.090
IQ		−.233	−.011	−.108	−.011	−.053	−.258	.159	.175
SES			−.201	−.101	−.081	.030	.072	−.133	−.106
MC				−.161	.135	.125	.137	.167	−.012
In-T					.301*	−.437*	−.021	−.092	.109
Ex-T						−.214	.110	.014	.041
FAA							.316*	.359*	−.097
LFAA								.053	−.035
CAA									465*

Note: IQ = Intelligence quotient; SES = socioeconomic status; MC = motor competence; In-T = internalizing problems adjusted T-scores; Ex- T = externalizing problems adjusted T-scores; FAA = frontal alpha asymmetry; CAA = central alpha asymmetry; LFAA = lateral frontal alpha asymmetry; PAA = parietal alpha asymmetry; * p < .05.

Table 3
Participant descriptors for each group (SE).

Variable	50 EG	30 EG	CG	*p*-value
Sample size	14	15	17	
Females	0	0	1	
Left-handed	1	1	2	
Taking medication	7	10	8	
Age (years)	10.1 (0.6)	9.6 (0.4)	10.4 (0.4)	.458
Weight (kg)	39.0 (3.4)	31.1 (2.2)	38.3 (2.7)	.175
Height (cm)	142.0 (11.4)	136.5 (10.1)	143.5 (10.9)	.079
IQ (percentile)	67.2 (7.7)	41.2 (7.2)	57.6 (7.7)	.060
SES (ISP scores)	25.9 (1.6)	28.1 (2.2)	30.0 (2.2)	.379
In-T#	58.0 (3.0)	64.5 (2.1)	64.4 (2.2)	.114
Ex-T#	64.9 (2.3)	69.8 (2.0)	66.0 (2.6)	.114
MC (standard scores)	11.1 (0.7)	9.9 (0.8)	10.7 (0.7)	.269
Resting HR	86.3 (2.1)	86.5 (2.5)	84.6 (2.5)	.853

Note. 50 EG = 50-minute exercise group; 30 EG = 30-minute exercise group; CG = control group; IQ = Intelligence quotient; SES = socioeconomic status; ISP = Index of Social Position; In-T = internalizing problems adjusted T-scores; Ex-T = externalizing problems adjusted T-scores; #CBCL data of three participants, specifically one in the CG and two in the 30 EG, were missing.

= .151). Thus, increased left-side frontal activity predominantly contributed to the effects of 50-minute AE on FAA.

Control analyses found no significant differences in post-test LFAA(F(2,42) = .422, p = .659, η^2_p = .02), post-test CAA (F(2,42) = .091, p = .913, η^2_p = .004), and post-test PAA (F(2,42) = 1.433, p = .250, η^2_p = .064) among the three groups, after adjusting for baseline values. All pre- and post-test EEG indices are shown in Table 4, and EEG topographic maps of the differences between post- and pre-test alpha powers for each group are presented in Fig. 2. Pre- and post-test alpha band results for each group are presented in the **supplementary document 3**.

3.4. Additional analyses

Control analyses indicated no significant difference in FAA (t (44) = −1.38, p = .174) between participants taking and not taking medication, indicating that medication use did not affect the results. Given that only one female and three left-handed participants were included in this study, we performed an additional analysis excluding these participants, similarly examining the association

Table 4
Alpha powers for all groups (SE).

Group	50 EG		30 EG		CG		*Effect size (η^2_p)
Indices/Time	Pre	Post	Pre	Post	Pre	Post	
FAA	0.018 (0.032)	0.117 (0.068)	0.027 (0.020)	−0.007 (0.031)	0.043 (0.023)	0.007 (0.034)	0.148
LFAA	−0.018 (0.050)	−0.129 (0.081)	−0.042 (0.042)	−0.098 (0.056)	0.018 (0.044)	−0.244 (0.067)	0.02
CAA	0.229 (0.105)	0.165 (0.111)	0.018 (0.062)	0.032 (0.043)	0.132 (0.063)	0.133 (0.062)	0.004
PAA	0.262 (0.100)	0.381 (0.100)	0.146 (0.065)	0.188 (0.074)	0.274 (0.091)	0.279 (0.089)	0.064

Note. * Effect size for ANCOVA while controlling for pre-test value. 50 EG = 50-minute exercise group; 30 EG = 30-minute exercise group; CG = control group; FAA = frontal alpha asymmetry; LFAA = lateral frontal alpha asymmetry; CAA = central alpha asymmetry; PAA = parietal alpha asymmetry.

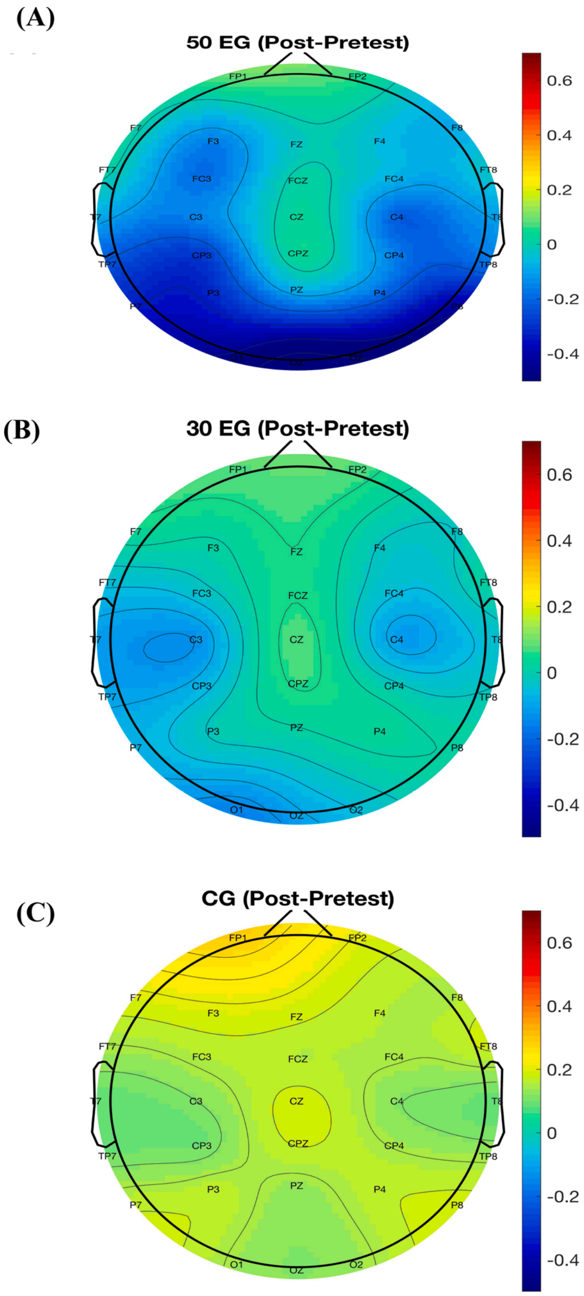

Fig. 2. Topography map of alpha power ($\mu V^2/cm^2$) for post-pretest differences in each group.
Note. Dark blue represents higher cortical activity (lower alpha power) for post-pretest differences.

between asymmetry indices and behavior problems and the effect of acute exercise on FAA, and the results were not altered.

To demonstrate the frequency specificity of our results, per the recommendations of Crabbe and Dishman (2004), we further analyzed different frequency band asymmetries in the frontal regions (F4 and F3), including frontal delta (1–3 Hz) asymmetry (FDA), frontal theta (4–7 Hz) asymmetry (FTA), frontal beta (13–30 Hz) asymmetry (FBA), frontal low-beta (13–20 Hz) asymmetry (FLBA), and frontal high-beta (21–30 Hz) asymmetry (FHBA). The results showed that these EEG indices were not significantly related to In-T, and only FLBA was affected by acute exercise. As such, we did not discuss the FLBA effect in this study due to the limited clinical implications. More detailed information on these analyses can be found in **supplementary document 4**.

4. Discussion

4.1. Summary of findings

The present study found that resting CSD-transformed FAA was negatively associated with the presence of internalizing psychological problems in children with ADHD. This association results from changes in the activity of both frontal hemispheres (reduced left-side frontal activity and increased right-side frontal activity). No relationship was found between internalizing problems and LFAA, CAA, or PAA. Additionally, we found that a 50-minute bout of AE resulted in higher FAA than either a 30-minute bout of AE or no exercise, after adjusting for baseline FAA. Moreover, the beneficial effect of the 50-minute AE intervention was found to result predominately from alterations to the left-side frontal area. No group effect was seen for LFAA, CAA, or PAA. Overall, the results of the current study provide novel evidence surrounding the role of FAA as a marker of internalizing problem and indicate that a 50-minute bout of AE is a viable way to modulate FAA via increased left-sided FAA dominance in children with ADHD.

4.1.1. Association of FAA with internalizing problems in children with ADHD

Our initial result that FAA was negatively associated with internalizing problems in children with ADHD is consistent with previous studies. Stewart et al. (2010) identified FAA as an endophenotype for depression risk in adults. Previous studies have similarly reported that lower FAA is associated with internalizing disorders such as depression or anxiety in adolescents and young adults (Feldmann et al., 2018; Kemp et al., 2010). Although the association between FAA and internalizing problems was found to be modest ($d = .19$) in healthy children (Peltola et al., 2014), no previous studies have examined the association between FAA and internalizing problems in children with ADHD. Additionally, the current study used a CSD analysis, which improved topographical localization and minimized volume conduction effects to provide a more precise measurement of FAA (Smith et al., 2017), particularly in the resting condition. Based on the capability model (Coan, Allen, & McKnight, 2006; Stewart et al., 2014), when data are referenced to traditional EEG references (i.e., average, Cz, and linked mastoid), FAA during emotional challenge is a stronger predictor of lifetime internalizing symptoms (e.g., major depressive disorder) than FAA during resting conditions. In contrast, both in-task and resting-state FAA are robust predictors of the lifetime internalizing status when asymmetry is quantified using a CSD-transformed method (Stewart et al., 2010, 2014). Moreover, the findings of current study demonstrated region specificity, with no associations seen between internalizing problems and other alpha asymmetry indices (LFAA, CAA, and PAA). As such, we provide strong evidence to support the use of CSD-transformed FAA under a resting state as a robust indicator of internalizing behaviors in children with ADHD.

Notably, internalizing problems were negatively associated with left-side frontal activity and positively associated with right-side frontal cortical activity. This suggests that children with ADHD with greater left-side frontal cortical activity (lower alpha power) and lower right-side frontal cortical activity (higher alpha power) have lower internalizing scores than those with lower left-side frontal cortical activity (greater alpha power) and greater right-side frontal cortical activity (lower alpha power). According to the updated approach-withdrawal motivational model (Harmon-Jones & Gable, 2017), left-side frontal areas are primarily associated with positively or negatively valenced approach motivations, whereas right-side frontal areas are associated with withdrawal motivations. Internalizing problems manifest as several withdrawal motivation symptoms including anxiety, depression, and psychosomatic reactions (for review, see Shankman & Klein, 2003). Thus, our results suggests that motivation regulation, as reflected by FAA, may play a role in the regulation of internalizing psychopathologies in children with ADHD.

4.1.2. Effect of acute exercise duration on FAA in children with ADHD

Regarding the acute effects of AE on FAA, the results support this study's hypothesis that, in children with ADHD, a 50-minute bout of moderate-intensity AE yields a larger effect relative to a 30-minute moderate-intensity AE. Moreover, it is likely that the left frontal hemisphere contributes more to this exercise-induced effect. Several previous studies have reported that 30 min of acute moderate-intensity AE positively affected FAA (Hicks et al., 2018; Woo et al., 2009, 2010). Woo et al. (2009) similarly reported the contribution of left-side frontal activity to this exercise-associated effect, but reported that a 30-minute bout of moderate-intensity AE resulted in a greater positive effect on FAA and vigor (assessed by self-reported affect) than either a 45-minute bout of AE, a 15-minute bout of AE, or no-exercise condition, in healthy young adults.

The discrepancies between our findings and previously reported studies may be due to differences in experimental design, the participants' clinical status, and age. For example, Woo et al. (2009) used a post-test comparison design, which did not control for day-to-day variations in FAA or any potential changes related to differences in baseline psychological/physiological states (Petruzzello & Landers, 1994; Petruzzello & Tate, 1997). The current study controlled for this, using pre-test scores as a covariate.

Studies have found that individuals suffering from internalizing problems demonstrated smaller changes in FAA in response to emotional challenge compared to healthy adults (Stewart, Coan, Towers, & Allen, 2011, 2014). Given that studies have reported that exercise could be considered an emotion-eliciting event (Petruzzello & Landers, 1994; Petruzzello & Tate, 1997), clinical status may possibly moderate the effect of acute bouts of AE on FAA. Clinical symptoms in individuals with internalizing disorders and children with ADHD could be accounted for, at least in part, by dysfunction of the dopaminergic and serotonergic systems (Canli & Lesch, 2007; Paclt et al., 2005; Salgado-Pineda et al., 2005), which may in turn, affect the modulation of FAA. Moreover, the downstream effects of the dopaminergic and serotonergic systems on frontal lobe function may depend on the integrity of the monoaminergic system (Celada et al., 2013; Schultz et al., 1998). Thus, individuals with impairments in the monoaminergic system, such as ADHD, may experience attenuated downstream effects of the dopaminergic and serotonergic systems on the frontal lobe. Indeed, children with ADHD have reduced dopaminergic responses to 30-minute bouts of AE relative to their age-matched neurotypical peers, suggesting a deficiency in their dopaminergic system (Wigal et al., 2003). As such, it might be possible that increased periods of exercise are required to normalize the activation of the dopaminergic system in children with ADHD, which supports our findings that favor a 50-minute bout of acute AE over a 30-minute bout of AE. Our findings also align with previous studies in adults that found that 35–60 min of AE resulted in positive effects on individuals with internalizing disorders (Brand et al., 2018; Herring et al., 2019). Moreover, post-exercise FAA has been reported to be related to a positive affective state in adults (Petruzzello et al., 2001; Woo et al., 2009, 2010). Accordingly, the current study suggest that longer AE is necessary to facilitate post-exercise FAA responses in individuals with high levels of internalizing symptoms, such as ADHD. Another alternative explanation to the null effect of a 30-minute bout of AE could be that our participants were too young to benefit from a short duration of exercise, as several studies have reported a positive effect of 30-minute AE on FAA and affective responses in young adults (Petruzzello et al., 2001; Woo et al., 2009, 2010). However, monoaminergic systems mature from childhood to adulthood, especially in ADHD (El-Sayed, Larsson, Persson, Santosh, & Rydelius, 2003). Future research that examines the dose-related effects of acute exercise on FAA modulation while taking age-related differences into account may address this issue.

4.2. Future implications

The present study first identified the relationship between FAA and internalizing problems, and subsequently showed that longer acute bouts of AE transiently increased FAA in children with ADHD. FAA is associated with monoamine neurotransmitter systems (Mann et al., 1996; Wacker et al., 2013) thought to be related to the pathophysiology of internalizing problems (Canli & Lesch, 2007; Salgado-Pineda et al., 2005). Based on animal studies, improved monoamine neurotransmitter system function may be achieved by repetitively increasing monoamine levels through acute bouts of exercise (for review, see Wegner et al., 2014). Neurofeedback training studies that aimed to increase FAA have reported that increased FAA was accompanied by reduced internalizing symptoms (Harmon-Jones et al., 2008; Mennella et al., 2017; Peeters et al., 2014). These results imply that repeatedly increasing FAA via an acute intervention is a potential approach to alleviate internalizing problems. Moreover, evidence from long-term exercise interventions support these findings. For example, children with ADHD who engaged in a 45-minute exercise intervention for 10 weeks (three times per week) had fewer internalizing problems compared with those who did not engage in exercise (Verret, Guay, Berthiaume, Gardiner, & Béliveau, 2012). Similar results were found with a 70-minute exercise intervention for 12 weeks (twice a week) (Pan et al., 2016). Hong et al. (2020) found that adolescents with internet gaming disorder displayed improved affect and enhanced FAA, resulting primarily from increased left-side frontal activity following an intervention of 60-minute moderate-intensity AE for 14 weeks. Collectively, there are important clinical implications of this study. Given that relatively longer periods of acute AE are effective for modulating FAA, this longer AE duration should be recommended when designing long-term exercise interventions with the aim of mitigating internalizing problems in children with ADHD.

4.3. Limitations

There are several limitations to the current study. First, there is a possibility that the medications being taken by the participants acted as a confounding factor due to differences in dosage. Nevertheless, the participants were required to refrain from medication for at least 24 h prior to the study to reduce such effects. Additionally, no differences in pre-test FAA were found between the participants taking and not taking medication. Second, despite using a randomized pretest-posttest design to examine the effects of acute exercise on FAA, the first research question was addressed using only pre-test FAA and internalizing problem data. As such, we could not determine any causal relationship between FAA and internalizing problems. Therefore, we recommend that future studies use longitudinal experimental designs to monitor changes in FAA and internalizing problems at several time points. Third, given that this study recruited only one female participant, it is not clear to what extent these results generalize to females, and it is recommended that future researchers recruit a wider range of subjects to address this issue. Fourth, we only examined the effects of acute AE on FAA. Whether our results generalize to other types of exercise such as exergaming, a form of AE involving hand-eye coordination exercises (Benzing, Chang, & Schmidt, 2018); Tai Chi Chuan (Wu et al., 2018), a form of traditional Chinese, low impact, mind-body exercise; or resistance exercises (Hsieh, Chang, Hung, & Fang, 2016; Wang et al., 2019) needs to be independently examined. Fifth, although the current study used an age-based HRmax method (207 – [0.7 × age]) for effectively setting HR range at target intensity during exercise (Gellish et al., 2007), HRmax can be estimated more accurately determined by VO_2 peak tests (American College of Sports Medicine, 2018). Future studies are encouraged to use this method. Finally, although we used a version of CSD transformation (Kayser & Tenke, 2006) that has also been demonstrated to offer sufficiently precise estimation in relatively low electrode-density recordings such as ours (i.e., 32 channels), studies suggested that high-density recordings (>64 channels) are required to guarantee accuracy of surface Laplacian estimates (Junghöfer, Elbert, Leiderer, Berg, & Rockstroh, 1997; Kayser & Tenke, 2015).

5. Conclusions

Our findings identify FAA as a clinical biomarker of internalizing problems in children with ADHD. We demonstrated that longer periods of acute AE may be a practical approach to increase left-sided FAA dominance in these children.

Funding information

This work is supported by the Institute for Research Excellence in Learning Sciences of National Taiwan Normal University (NTNU) within the framework of the Higher Education Sprout Project by the Ministry of Education (MOE) in Taiwan, and by the Ministry of

Science and Technology (MOST).

CRediT authorship contribution statement

Ting-Yu Chueh: Conceptualization, Data curation, Formal analysis, Methodology, Project administration, Writing - original draft. **Shu-Shih Hsieh:** Formal analysis, Project administration, Writing - review & editing. **Yu-Jung Tsai:** Formal analysis, Methodology, Project administration. **Chien-Lin Yu:** Formal analysis, Project administration. **Chung-Ju Huang:** Conceptualization, Methodology, Resources, Supervision, Writing - review & editing. **Tsung-Min Hung:** Conceptualization, Data curation, Funding acquisition, Methodology, Resources, Software, Supervision, Writing - review & editing.

Declaration of Competing Interest

There is no conflict of interest to report.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.ridd.2021.104063.

References

Achenbach, T., & Rescorla, L. (2001). *Manual for the ASEBA school-age forms & profiles: An integrated system of multi-informant assessment. University of vermont.* Research Center for Children, Youth, & Families.

Albores-Gallo, L., Lara-Muñoz, C., Esperón-Vargas, C., Zetina, J., Soriano, A., & Colin, G. V. (2007). *Validity and reliability of the CBCL/6-18. Includes DSM scales*. Actas espanolas de psiquiatria.

Allen, J. J., Coan, J. A., & Nazarian, M. (2004). Issues and assumptions on the road from raw signals to metrics of frontal EEG asymmetry in emotion. *Biological Psychology, 67*(1-2), 183–218.

American College of Sports Medicine. (2010). *ACSM's guidelines for exercise testing and prescription* (8th ed.). Lippincott williams & wilkins.

American College of Sports Medicine. (2018). *ACSM's guidelines for exercise testing and prescription* (10th ed.). Lippincott williams & wilkins.

Basso, J. C., & Suzuki, W. A. (2017). The effects of acute exercise on mood, cognition, neurophysiology, and neurochemical pathways: A review. *Brain Plasticity, 2*(2), 127–152.

Bell, A. J., & Sejnowski, T. J. (1995). An information-maximization approach to blind separation and blind deconvolution. *Neural Computation, 7*(6), 1129–1159.

Benzing, V., Chang, Y.-K., & Schmidt, M. (2018). Acute physical activity enhances executive functions in children with ADHD. *Scientific Reports, 8*(1), 12382.

Blackman, G. L., Ostrander, R., & Herman, K. C. (2005). Children with ADHD and depression: A multisource, multimethod assessment of clinical, social, and academic functioning. *Journal of Attention Disorders, 8*(4), 195–207. https://doi.org/10.1177/1087054705278777.

Brand, S., Colledge, F., Ludyga, S., Emmenegger, R., Kalak, N., Sadeghi Bahmani, D., et al. (2018). Acute bouts of exercising improved mood, rumination and social interaction in inpatients with mental disorders. *Frontiers in Psychology, 9*, 249.

Brown, L., Sherbenou, R. J., & Johnsen, S. K. (1990). *Test of Nonverbal Intelligence: A language-free measure of cognitive ability*. Pro-ed Austin, TX.

Canli, T., & Lesch, K.-P. (2007). Long story short: The serotonin transporter in emotion regulation and social cognition. *Nature Neuroscience, 10*(9), 1103–1109.

Carvalhaes, C., & de Barros, J. A. (2015). The surface Laplacian technique in EEG: Theory and methods. *International Journal of Psychophysiology, 97*(3), 174–188.

Celada, P., Puig, M., & Artigas, F. (2013). Serotonin modulation of cortical neurons and networks. *Frontiers in Integrative Neuroscience, 7*, 25.

Chang, Y.-K., Liu, S., Yu, H.-H., & Lee, Y.-H. (2012). Effect of acute exercise on executive function in children with attention deficit hyperactivity disorder. *Archives of Clinical Neuropsychology, 27*(2), 225–237. https://doi.org/10.1093/arclin/acr094.

Chen, E., Huang, H., & Chao, C. (2006). *ASEBA: Achenback system of empirically based assessment*. Taipei: Psychological Publishing.

Coan, J. A., Allen, J. J., & McKnight, P. E. (2006). A capability model of individual differences in frontal EEG asymmetry. *Biological Psychology, 72*(2), 198–207.

Crabbe, J. B., & Dishman, R. K. (2004). Brain electrocortical activity during and after exercise: A quantitative synthesis. *Psychophysiology, 41*(4), 563–574.

Delorme, A., & Makeig, S. (2004). EEGLAB: An open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *Journal of Neuroscience Methods, 134*(1), 9–21. https://doi.org/10.1016/j.jneumeth.2003.10.009.

El-Sayed, E., Larsson, J. O., Persson, H., Santosh, P., & Rydelius, P. A. (2003). "Maturational lag" hypothesis of attention deficit hyperactivity disorder: an update. *Acta Paediatrica, 92*(7), 776–784.

Faul, F., Erdfelder, E., Buchner, A., & Lang, A.-G. (2009). Statistical power analyses using G* Power 3.1: Tests for correlation and regression analyses. *Behavior Research Methods, 41*(4), 1149–1160.

Feldmann, L., Piechaczek, C. E., Grünewald, B. D., Pehl, V., Bartling, J., Frey, M., et al. (2018). Resting frontal EEG asymmetry in adolescents with major depression: Impact of disease state and comorbid anxiety disorder. *Clinical Neurophysiology, 129*(12), 2577–2585. https://doi.org/10.1016/j.clinph.2018.09.028.

Gellish, R. L., Goslin, B. R., Olson, R. E., McDONALD, A., Russi, G. D., & Moudgil, V. K. (2007). Longitudinal modeling of the relationship between age and maximal heart rate. *Medicine and Science in Sports and Exercise, 39*(5), 822–829.

Hagemann, D. (2004). Individual differences in anterior EEG asymmetry: Methodological problems and solutions. *Biological Psychology, 67*(1–2), 157–182.

Harmon-Jones, E., & Gable, P. A. (2017). On the role of asymmetric frontal cortical activity in approach and withdrawal motivation: An updated review of the evidence. *Psychophysiology, 55*(1), e12879. https://doi.org/10.1111/psyp.12879.

Harmon-Jones, E., Harmon-Jones, C., Fearn, M., Sigelman, J. D., & Johnson, P. (2008). Left frontal cortical activation and spreading of alternatives: Tests of the action-based model of dissonance. *Journal of Personality and Social Psychology, 94*(1), 1.

Henderson, S. E., Sugden, D. A., & Barnett, A. L. (2007). *Movement assessment battery for Children-2: MABC-2*. Pearson Assessment.

Herring, M. P., Monroe, D. C., Gordon, B. R., Hallgren, M., & Campbell, M. J. (2019). Acute exercise effects among young adults with analogue generalized anxiety disorder. *Medicine and Science in Sports and Exercise, 51*(5), 962.

Hicks, R. A., Hall, P. A., Staines, W. R., & McIlroy, W. E. (2018). Frontal alpha asymmetry and aerobic exercise: are changes due to cardiovascular demand or bilateral rhythmic movement? *Biological Psychology, 132*, 9–16. https://doi.org/10.1016/j.biopsycho.2017.10.011.

Hollingshead. (1957). *Hollingshead two factor index of social position Handbook of Research Design and Social Measurement* (5th ed., pp. 351–359). Newbury Park, CA: Sage Publications.

Hong, J. S., Kim, S. M., Kang, K. D., Han, D. H., Kim, J. S., Hwang, H., et al. (2020). Effect of physical exercise intervention on mood and frontal alpha asymmetry in internet gaming disorder. *Mental Health and Physical Activity*. , Article 100318. https://doi.org/10.1016/j.mhpa.2020.100318.

Hsieh, S.-S., Chang, Y.-K., Hung, T.-M., & Fang, C.-L. (2016). The effects of acute resistance exercise on young and older males' working memory. *Psychology of Sport and Exercise, 22*, 286–293. https://doi.org/10.1016/j.psychsport.2015.09.004.

Hulley, S., Cummings, S., Browner, W., Grady, D., & Newman, T. (2013). *Designing clinical research* (vol. 4th). Philadelphia: LWW.

Jerrell, J. M., McIntyre, R. S., & Park, Y.-M. M. (2015). Risk factors for incident major depressive disorder in children and adolescents with attention-deficit/hyperactivity disorder. *European Child & Adolescent Psychiatry, 24*(1), 65–73.

Junghöfer, M., Elbert, T., Leiderer, P., Berg, P., & Rockstroh, B. (1997). Mapping EEG-potentials on the surface of the brain: A strategy for uncovering cortical sources. *Brain Topography, 9*(3), 203–217.

Kang, N., You, J., Huang, J., Ren, Y., Lin, M.p., & Xu, S. (2019). Understanding the pathways from depression to suicidal risk from the perspective of the interpersonal–Psychological theory of suicide. *Suicide and Life-Threatening Behavior, 49*(3), 684–694. https://doi.org/10.1111/sltb.12455.

Kayser, J., & Tenke, C. E. (2006). Principal components analysis of Laplacian waveforms as a generic method for identifying ERP generator patterns: II. Adequacy of low-density estimates. *Clinical Neurophysiology, 117*(2), 369–380. https://doi.org/10.1016/j.clinph.2005.08.033.

Kayser, J., & Tenke, C. E. (2015). Issues and considerations for using the scalp surface Laplacian in EEG/ERP research: A tutorial review. *International Journal of Psychophysiology, 97*(3), 189–209.

Kemp, A., Griffiths, K., Felmingham, K., Shankman, S. A., Drinkenburg, W., Arns, M., et al. (2010). Disorder specificity despite comorbidity: Resting EEG alpha asymmetry in major depressive disorder and post-traumatic stress disorder. *Biological Psychology, 85*(2), 350–354. https://doi.org/10.1016/j.biopsycho.2010.08.001.

Kline, R. B. (2015). *Principles and practice of structural equation modeling.* Guilford publications.

Lattari, E., Portugal, E., Junior, R. S. M., Oliveira, B. R. R., Santos, T. M., Mura, G., et al. (2016). Acute affective responses and frontal electroencephalographic asymmetry to prescribed and self-selected exercise. *Clinical Practice and Epidemiology in Mental Health: CP & EMH, 12*, 108.

Laufs, H., Kleinschmidt, A., Beyerle, A., Eger, E., Salek-Haddadi, A., Preibisch, C., et al. (2003). EEG-correlated fMRI of human alpha activity. *Neuroimage, 19*(4), 1463–1476.

Leirbakk, M. J., Clench-Aas, J., & Raanaas, R. K. (2015). ADHD with co-occurring depression/anxiety in children: The relationship with somatic complaints and parental socio-economic position. *Journal of Psychological Abnormalities in Children*. https://doi.org/10.4172/2329-9525.1000137.

Lin, M. P., You, J., Wu, Y. W., & Jiang, Y. (2018). Depression mediates the relationship between distress tolerance and nonsuicidal self-injury among adolescents: One-year follow-up. *Suicide and Life-Threatening Behavior, 48*(5), 589–600. https://doi.org/10.1111/sltb.12382.

Mann, J. J., Malone, K. M., Diehl, D. J., Perel, J., Nichols, T. E., & Mintun, M. A. (1996). Positron emission tomographic imaging of serotonin activation effects on prefrontal cortex in healthy volunteers. *Journal of Cerebral Blood Flow & Metabolism, 16*(3), 418–426.

Marshall, R., & Mardia, K. (1985). Minimum norm quadratic estimation of components of spatial covariance. *Journal of the International Association for Mathematical Geology, 17*(5), 517–525.

Mennella, R., Patron, E., & Palomba, D. (2017). Frontal alpha asymmetry neurofeedback for the reduction of negative affect and anxiety. *Behaviour Research and Therapy, 92*, 32–40.

Mikami, A. Y., Ransone, M. L., & Calhoun, C. D. (2011). Influence of anxiety on the social functioning of children with and without ADHD. *Journal of Attention Disorders, 15*(6), 473–484. https://doi.org/10.1177/1087054710369066.

Nuwer, M. R., Lehmann, D., da Silva, F. L., Matsuoka, S., Sutherling, W., & Vibert, J. (1999). IFCN guidelines for topographic and frequency analysis of EEGs and EPs. The International Federation of Clinical Neurophysiology. *Electroencephalography and Clinical Neurophysiology. Supplement, 52*, 15–20.

Oakes, T. R., Pizzagalli, D. A., Hendrick, A. M., Horras, K. A., Larson, C. L., Abercrombie, H. C., et al. (2004). Functional coupling of simultaneous electrical and metabolic activity in the human brain. *Human Brain Mapping, 21*(4), 257–270.

Ohmatsu, S., Nakano, H., Tominaga, T., Terakawa, Y., Murata, T., & Morioka, S. (2014). Activation of the serotonergic system by pedaling exercise changes anterior cingulate cortex activity and improves negative emotion. *Behavioural Brain Research, 270*, 112–117.

Paclt, I., Koudelová, J., Krepelova, A., Uhlíková, P., Gazdíková, M., & Bauer, P. (2005). Biochemical markers and genetic research of ADHD. *Neuro Endocrinol Letters, 26*(4), 423–430.

Pan, C.-Y., Chu, C.-H., Tsai, C.-L., Lo, S.-Y., Cheng, Y.-W., & Liu, Y.-J. (2016). A racket-sport intervention improves behavioral and cognitive performance in children with attention-deficit/hyperactivity disorder. *Research in Developmental Disabilities, 57*, 1–10.

Peeters, F., Ronner, J., Bodar, L., van Os, J., & Lousberg, R. (2014). Validation of a neurofeedback paradigm: Manipulating frontal EEG alpha-activity and its impact on mood. *International Journal of Psychophysiology, 93*(1), 116–120.

Peltola, M. J., Bakermans-Kranenburg, M. J., Alink, L. R., Huffmeijer, R., Biro, S., & van IJzendoorn, M. H. (2014). Resting frontal EEG asymmetry in children: Meta-analyses of the effects of psychosocial risk factors and associations with internalizing and externalizing behavior. *Developmental Psychobiology, 56*(6), 1377–1389. https://doi.org/10.1002/dev.21223.

Perrin, F., Pernier, J., Bertrand, O., & Echallier, J. (1989). Spherical splines for scalp potential and current density mapping. *Electroencephalography and Clinical Neurophysiology, 72*(2), 184–187.

Petruzzello, S. J., & Landers, D. M. (1994). State anxiety reduction and exercise: does hemispheric activation reflect such changes? *Medicine & Science in Sports & Exercise*.

Petruzzello, S. J., & Tate, A. K. (1997). Brain activation, affect, and aerobic exercise: An examination of both state-independent and state-dependent relationships. *Psychophysiology, 34*(5), 527–533.

Petruzzello, S. J., Hall, E. E., & Ekkekakis, P. (2001). Regional brain activation as a biological marker of affective responsivity to acute exercise: Influence of fitness. *Psychophysiology, 38*(1), 99–106.

Pivik, R. T., Broughton, R. J., Coppola, R., Davidson, R. J., Fox, N., & Nuwer, M. R. (1993). Guidelines for the recording and quantitative analysis of electroencephalographic activity in research contexts. *Psychophysiology, 30*(6), 547–558.

Pontifex, M. B., Miskovic, V., & Laszlo, S. (2017). Evaluating the efficacy of fully automated approaches for the selection of eyeblink ICA components. *Psychophysiology, 54*(5), 780–791. https://doi.org/10.1111/psyp.12827.

Pontifex, M. B., Saliba, B. J., Raine, L. B., Picchietti, D. L., & Hillman, C. H. (2013). Exercise improves behavioral, neurocognitive, and scholastic performance in children with attention-deficit/hyperactivity disorder. *The Journal of Pediatrics, 162*(3), 543–551.

Reznik, S. J., & Allen, J. J. (2018). Frontal asymmetry as a mediator and moderator of emotion: An updated review. *Psychophysiology, 55*(1), e12965. https://doi.org/10.1111/psyp.12965.

Salgado-Pineda, P., Delaveau, P., Blin, O., & Nieoullon, A. (2005). Dopaminergic contribution to the regulation of emotional perception. *Clinical Neuropharmacology, 28*(5), 228–237.

Schultz, W., Tremblay, L., & Hollerman, J. R. (1998). Reward prediction in primate basal ganglia and frontal cortex. *Neuropharmacology, 37*(4-5), 421–429.

Sciberras, E., Lycett, K., Efron, D., Mensah, F., Gerner, B., & Hiscock, H. (2014). Anxiety in children with attention-deficit/hyperactivity disorder. *Pediatrics*, 2013–3686. https://doi.org/10.1542/peds.2013-3686. peds.

Shankman, S. A., & Klein, D. N. (2003). The relation between depression and anxiety: An evaluation of the tripartite, approach-withdrawal and valence-arousal models. *Clinical Psychology Review, 23*(4), 605–637.

Shea, C. K., Lee, M. M., Lai, K. Y., Luk, E. S., & Leung, P. W. (2018). Prevalence of anxiety disorders in Hong Kong Chinese children with ADHD. *Journal of Attention Disorders, 22*(5), 403–413.

Silveira, R., Prado, R. C. R., Brietzke, C., Coelho-Júnior, H. J., Santos, T. M., Pires, F. O., et al. (2019). Prefrontal cortex asymmetry and psychological responses to exercise: A systematic review. *Physiology & Behavior, 208*, Article 112580.

Smith, E. E., Reznik, S. J., Stewart, J. L., & Allen, J. J. (2017). Assessing and conceptualizing frontal EEG asymmetry: An updated primer on recording, processing, analyzing, and interpreting frontal alpha asymmetry. *International Journal of Psychophysiology, 111*, 98–114. https://doi.org/10.1016/j.ijpsycho.2016.11.005.

Stewart, J. L., Bismark, A. W., Towers, D. N., Coan, J. A., & Allen, J. J. (2010). Resting frontal EEG asymmetry as an endophenotype for depression risk: Sex-specific patterns of frontal brain asymmetry. *Journal of Abnormal Psychology, 119*(3), 502. https://doi.org/10.1037/a0019196.

Stewart, J. L., Coan, J. A., Towers, D. N., & Allen, J. J. (2011). Frontal EEG asymmetry during emotional challenge differentiates individuals with and without lifetime major depressive disorder. *Journal of Affective Disorders, 129*(1-3), 167–174.

Stewart, J. L., Coan, J. A., Towers, D. N., & Allen, J. J. (2014). Resting and task-elicited prefrontal EEG alpha asymmetry in depression: Support for the capability model. *Psychophysiology, 51*(5), 446–455.

Thomas, R., Sanders, S., Doust, J., Beller, E., & Glasziou, P. (2015). Prevalence of attention-deficit/hyperactivity disorder: A systematic review and meta-analysis. *Pediatrics, 135*(4), e994–e1001.

Tomarken, A. J., Davidson, R. J., Wheeler, R. E., & Kinney, L. (1992). Psychometric properties of resting anterior EEG asymmetry: Temporal stability and internal consistency. *Psychophysiology, 29*(5), 576–592.

Utter, A. C., Robertson, R. J., Nieman, D. C., & Kang, J. (2002). Children's OMNI scale of perceived exertion: walking/running evaluation. *Medicine & Science in Sports & Exercise, 34*(1), 139–144.

Verret, C., Guay, M.-C., Berthiaume, C., Gardiner, P., & Béliveau, L. (2012). A physical activity program improves behavior and cognitive functions in children with ADHD: An exploratory study. *Journal of Attention Disorders, 16*(1), 71–80.

Volkow, N. D., Wang, G.-J., Newcorn, J. H., Kollins, S. H., Wigal, T. L., Telang, F., et al. (2011). Motivation deficit in ADHD is associated with dysfunction of the dopamine reward pathway. *Molecular Psychiatry, 16*(11), 1147–1154.

Wacker, J. (2018). Effects of positive emotion, extraversion, and dopamine on cognitive stability-flexibility and frontal EEG asymmetry. *Psychophysiology, 55*(1), Article e12727.

Wacker, J., Mueller, E. M., Pizzagalli, D. A., Hennig, J., & Stemmler, G. (2013). Dopamine-D2-receptor blockade reverses the association between trait approach motivation and frontal asymmetry in an approach-motivation context. *Psychological Science, 24*(4), 489–497.

Wang, C.-C., Alderman, B., Wu, C.-H., Chi, L., Chen, S.-R., Chu, I.-H., et al. (2019). Effects of acute aerobic and resistance exercise on cognitive function and salivary cortisol responses. *Journal of Sport and Exercise Psychology, 41*(2), 73–81. https://doi.org/10.1123/jsep.2018-0244.

Wegner, M., Helmich, I., Machado, S., E Nardi, A., Arias-Carrion, O., & Budde, H. (2014). Effects of exercise on anxiety and depression disorders: Review of meta-analyses and neurobiological mechanisms. *CNS & Neurological Disorders-Drug Targets (Formerly Current Drug Targets-CNS & Neurological Disorders), 13*(6), 1002–1014.

Wigal, S. B., Nemet, D., Swanson, J. M., Regino, R., Trampush, J., Ziegler, M. G., et al. (2003). Catecholamine response to exercise in children with attention deficit hyperactivity disorder. *Pediatric Research, 53*(5), 756–761.

Woo, M., Kim, S., Kim, J., Petruzzello, S. J., & Hatfield, B. D. (2009). Examining the exercise-affect dose–response relationship: Does duration influence frontal EEG asymmetry? *International Journal of Psychophysiology, 72*(2), 166–172. https://doi.org/10.1016/j.ijpsycho.2008.12.003.

Woo, M., Kim, S., Kim, J., Petruzzello, S. J., & Hatfield, B. D. (2010). The influence of exercise intensity on frontal electroencephalographic asymmetry and self-reported affect. *Research Quarterly for Exercise and Sport, 81*(3), 349–359.

Wu, M.-T., Tang, P.-F., Goh, J. O., Chou, T.-L., Chang, Y.-K., Hsu, Y.-C., … Gau, S. S.-F. (2018). Task-switching performance improvements after Tai Chi Chuan training are associated with greater prefrontal activation in older adults. *Frontiers in Aging Neuroscience, 10*, 280. https://doi.org/10.3389/fnagi.2018.00280.

Wuang, Y. P., Su, J. H., & Su, C. Y. (2012). Reliability and responsiveness of the Movement Assessment Battery for Children–Second Edition Test in children with developmental coordination disorder. *Developmental Medicine & Child Neurology, 54*(2), 160–165.