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Effectiveness of a Brain-Computer Interface Based Programme for the Treatment of ADHD: A Pilot Study

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ABSTRACT ~ Majority of children with attention deficit hyperactivity disorder (ADHD) have significant inattentive symptoms. We developed a progressive series of activities involving brain-computer interface-based games which could train users to improve their concentration. This pilot study investigated if the intervention could be utilized in children and if it could improve inattentive symptoms of ADHD. Ten medication-naïve children aged 7 to 12 diagnosed with ADHD (combined or inattentive subtypes) received 20 sessions of therapy over a 10-week period. They were compared with age- and gender-matched controls. Both parent and teacher-rated inattentive score on the ADHD Rating Scale-IV improved more in the intervention group. A larger scale trial is warranted to further investigate the efficacy of our treatment programme in treating ADHD. Psychopharmacology Bulletin. 2010;43(1):00-00.

INTRODUCTION

Worldwide, attention-deficit hyperactivity disorder (ADHD) is common with an estimated prevalence rate of 5.29%.¹ ADHD is characterised by childhood onset of pervasive inattentive and/or hyperactive-impulsive symptoms. Although these symptoms decline with age,² up to half of the children continue to meet clinical diagnostic criteria in adulthood, especially for those with the combined

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and inattentive subtypes.³ Male-female ratios have been reported to be as high as 9:1 in clinical populations.⁴ ADHD leads to many negative outcomes including academic underachievement, low self-esteem, work difficulty, social rejection, driving accidents, substance misuse and criminality, making it an important public health problem with high economic burden^{5,6} In Singapore, ADHD ranks as the third highest cause of disease burden in youths below the age of 14.⁷

The main treatment modalities for ADHD include behavioural and pharmacological treatment. Behaviour management has been shown to be less effective than medication.⁸ Stimulant medications often cause significant side effects including poor appetite and physical growth suppression,⁸ and non-adherence rate can be as high as 25%.⁹ More recently, they have even been associated with sudden death.¹⁰ Although their mean effect size for treating ADHD symptoms is 0.78, it is a modest 0.34 for academic achievement.¹¹ Atomoxetine is less effective and carries a black box warning of causing suicidal ideation.^{12,13} Even with combined medication and intensive behavioural treatment, successful treatment rate only hovers around 68%.¹⁴ As Pelham opined, other interventions are needed for treatment non-responders or incomplete responders.¹⁵

Brain-computer interface (BCI) is the science and technology of devices and systems which directly respond to neural and cognitive processes.¹⁶ We have developed a progressive series of training games using electroencephalogram (EEG) based BCI. The BCI can quantify one's attention level as measured by EEG waves, thereby allowing users to employ their attention to play these games directly. Three-channel EEG signals are recorded from the frontal (Fp1, Fp2) and parietal (Pz) positions. These EEG signals first pass through a filter bank to be broken down into various frequency sub-bands covering the range from 4Hz to 36Hz (i.e. covering theta, alpha, beta 1, and beta 2 waves). The filtered signals are then sent to the respective spatial filters corresponding to each frequency band, which enhance the detection of information from the brain's electrical rhythm. We applied the machine learning method to derive a parametric model from the multi-band EEG signals, and then use this model to classify incoming EEG into attention or non-attention states, with a corresponding quantifiable score to indicate the subject's attention level.¹⁷ This model, built upon the EEG data collected during a calibration period when the subject is asked to perform attention and relaxation tasks, is subject-dependent and individualized. As the system makes use of a subject's direct attention to control a game, it works on a feed-forward mechanism. This small pilot study was completed to investigate the efficacy and feasibility of using our BCI-based training programme to treat inattentive symptoms of ADHD.

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METHODS

Ethics Statement

Approval for this study was obtained from the ethics review board of the National Healthcare Group, Singapore. Written informed consent from parents and assent from children were obtained prior to study entry.

Subjects

Ten children aged 7 to 12, who were seen at the clinic and diagnosed to have either the combined or inattentive subtype of ADHD based on the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) were recruited into the intervention group. These children were medication naive and referred for the study as their parents declined medication. Exclusion criteria for the study included (1) previous treatment with stimulant medication or atomoxetine, (2) presence of any comorbid severe psychiatric condition or known sensori-neural deficit such as complete blindness or deafness, (3) history of epileptic seizures and (4) known mental retardation (i.e. IQ 70 and below). Parents of these children underwent the Diagnostic Interview Schedule for Children Version IV (DISC-IV)¹⁸ before enrolment into the study. An additional 10 children with ADHD, who were matched for age and gender, whose parents similarly declined medication, were enrolled as controls.

Throughout the study, each child continued to receive their usual follow up with their treating doctor, who could prescribe any treatment that was required. Enrolment in the study did not preclude treatment with medication if the child's parent or the doctor felt it was necessary. At each clinic visit throughout the study period, parents were asked if the child received any additional intervention, medication or supplement which may affect the child's ADHD symptoms; if they did, they were considered a drop-out at that point.

Intervention Protocol

Participants in the intervention group underwent 2 individual BCI intervention sessions per week over a 10-week period, giving a total of 20 sessions each. The therapist was trained to position the EEG leads (Fp1, Fp2 and Pz positions with linked earlobe reference) and to administer the manualized intervention protocol. At the first session, each child would need to master a simple concentration (calibration) task involving a puzzle game. The game progressed at a speed proportional to the child's attention level. During subsequent sessions, the

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child played a series of games of increasing difficulty (see Figure 1). Each session lasted 30 minutes. The therapist adjusted the difficulty of each task so that the child remained engaged, and completed the entire training programme over 20 sessions according to the protocol. At the end of every alternate session, the child also completed 2 worksheets at their grade level, consisting of 10 Mathematics and 2 English comprehension questions, with the BCI system monitoring their attention level simultaneously. These worksheets were prepared by our clinic's experienced educational psychologist for each school grade and would take about 10 minutes for an average student to complete. There were 5 sets prepared for each grade from 1 to 6 respectively. These worksheets were administered serially and repeated after 10 weeks. This part of the intervention aimed to train the child to generalize their learnt 'concentration skill' to their daily academic work.

Assessment

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The subjects' parents and teachers completed the ADHD Rating Scale-IV¹⁹ at baseline, week 5 (intervention mid-point) and week 10

FIGURE 1

AN ILLUSTRATION OF A BCI-BASED INTERVENTION SESSION



(intervention completion). This is an 18-item questionnaire based on DSM-IV. The frequency of each symptom is rated on a 4-point scale. The questionnaire can be used for treatment outcome measures and has a high level of internal consistency and test-retest reliability. While parents could not be blinded to the intervention the children received, teachers were blinded. All parent-rated questionnaires were completed during clinic visits. Teacher-rated questionnaires were mailed to the child's school form teacher, which were returned after completion in a self-addressed envelop.

The primary outcome we analysed was the inattentive score on this rating scale at 10 weeks. Based on a treatment difference of 50% between the intervention and control groups, power of 80% and type I error of 5%, a sample size of 10 subjects per group is necessary. As the intervention was experimental, it was ethically necessary that subjects were told that they could decide to receive medication or other intervention during the trial but to inform the trial investigator should they do so. For such subjects, if they took medication after the week 5 rating scale result was obtained, this result would be carried forward to week 10 during analysis. If medication was taken before the week 5 assessment was completed, the subject would be excluded during analysis to avoid confounding caused by the additional intervention. We also did a sensitivity analysis based on the per-protocol principle whereby all subjects who took medication, regardless of timing, were excluded from the analysis. Statistical analysis was performed using the Statistical Package for the Social Sciences Version 17. The ADHD Rating Scale result was analysed using the Mann-Whitney U test.

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RESULTS

Eight boys and 2 girls per group were enrolled into the intervention and control group. There were 9 Chinese and 1 Indian in the intervention group whereas all 10 children in the control group were Chinese. The mean age of the 10 subjects in each group was 8.9 (SD 1.4). Eight subjects in the intervention group completed the 10-week intervention. Two boys dropped out after less than 5 intervention sessions due to difficulty making the clinic visits and were excluded during data analysis. Among the control group subjects, one dropped out due to an unrelated medical condition while another took stimulant medication before the week 5 assessment was conducted. Three controls took either stimulant medication or omega-3 fish oil supplement between week 5 and 10; thus, we used their week 5 ratings for the analysis at week 10.

Table 1 summarises the demographic characteristics and parent-rated ADHD Rating Scale scores for the participants included in the analysis. Both groups were similar in their baseline characteristics. Table 2

TABLE 1

CLINICAL DIAGNOSES, ADHD RATING SCALE IV (ARS-IV) INATTENTIVE (IA)
AND HYPERACTIVE-IMPULSIVE (HI) MEAN RAW SCORES AS RATED BY PARENTS

		INTERVENTION GROUP N = 8	CONTROL GROUP N = 8
Age		8.6 (1.4)	9.1 (1.5)
Gender	Male	6	7
	Female	2	1
ADHD Subtype	Combined	5	6
	Inattentive	3	2
ARS-IV IA	Baseline	18.0 (6.1)	17.9 (5.7)
	Week 5	17.8 (6.0)	18.4 (6.0)
	Week 10	15.0 (5.9)	18.6 (5.7)
	Change	-3.0 (4.8)	0.8 (1.3)
ARS-IV HI	Baseline	14.9 (5.6)	17.6 (5.0)
	Week 5	14.1 (5.7)	16.5 (5.1)
	Week 10	11.4 (4.6)	15.6 (5.7)
	Change	-3.5 (4.5)	-1.0 (1.7)

Results in () Denote the Standard Deviation.
Note that Higher Scores Denote Worse Symptoms.

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TABLE 2

CLINICAL DIAGNOSES, ADHD RATING SCALE IV (ARS-IV) INATTENTIVE (IA)
AND HYPERACTIVE-IMPULSIVE (HI) MEAN RAW SCORES AS RATED BY TEACHERS

		INTERVENTION GROUP N = 5	CONTROL GROUP N = 6
Age		8.2 (1.3)	9.0 (1.4)
Gender	Male	3	5
	Female	2	1
ARS-IV IA	Baseline	16.6 (9.7)	12.3 (3.6)
	Week 5	14.0 (8.3)	13.2 (4.3)
	Week 10	10.6 (9.0)	11.5 (4.8)
	Change	-6.0 (5.9)	-0.8 (5.6)
ARS-IV HI	Baseline	16.8 (9.3)	15.0 (6.1)
	Week 5	14.6 (7.7)	13.8 (6.4)
	Week 10	11.2 (7.3)	10.5 (4.8)
	Change	-5.6 (2.2)	-4.5 (7.6)

Results in () Denote the Standard Deviation.

summarises the teachers' ratings. The sample size was further reduced due to the teachers' higher non-response rate.

At week 10, the mean change in the parent-rated inattentive score on the ADHD Rating Scale was -3.0 (4.8) for the intervention group and 0.8 (1.3) for the control group, although the distributions in the two

groups did not differ significantly (Mann-Whitney $U = 16.000$, $n_1 = 8$, $n_2 = 8$, $p = 0.053$ one-tailed). Teacher-rated inattentive score showed a larger treatment difference between the 2 groups (Mann-Whitney $U = 5.000$, $n_1 = 5$, $n_2 = 6$, $p = 0.041$, one-tailed). Comparatively, the magnitude of the improvement in parent- and teacher-rated hyperactive-impulsive symptoms in the intervention group was smaller.

Sensitivity analysis using per-protocol set that included 8 and 5 participants in the intervention and control group respectively was performed. The mean change in parent-rated inattention score on the ADHD Rating Scale at 10 weeks compared to baseline was -3.0 (SD 4.8) and 1.0 (SD 1.4) for the intervention group and treatment group respectively (Mann-Whitney $U = 9.000$, $n_1 = 8$, $n_2 = 5$, $p = 0.064$ one-tailed).

DISCUSSION

Although data from this pilot study showed a larger improvement in inattentive scores over 10 weeks as rated both by parents and teachers in the intervention group, this difference did not reach statistical significance when compared with the control group. The magnitude of difference or effect size (difference in means divided by average of SDs) for parental ratings was about -0.95 SD (95% C.I. -1.92 to 0.01 SD), and that for teachers' ratings was -0.85 SD and (95% C.I. -2.14 to 0.44 SD). The small sample size could have affected the statistical power of our trial, and a larger study to further investigate the efficacy of the BCI intervention programme in treating inattentive symptoms of ADHD will be required. Both intervention and control groups improved in their hyperactive-impulsive symptoms, which could be related to being in a treatment programme.

Since the BCI device could calibrate itself against the user's 'maximum' attention level on a given task rather than use a preset level, our intervention had the advantage that there was no need for the child to undergo additional pre-intervention assessment for suitability. During the trial, the children completed the BCI-based training activities with relative ease, and both girls and boys progressed well through the same training programme. The intervention was well accepted by both the subjects and their parents. None of the children refused to turn up for the intervention, other than the 2 who had difficulties with scheduling either due to their school hours or parents' work commitment. Other than feeling fatigued by the end of an intervention session, there was no major adverse event reported by the children.

One potential problem which can limit the effectiveness of our intervention is the inconvenience caused by the frequent clinic visits required over a moderately long period of 10 weeks. This may result in high

drop-out rate. Although our study showed an encouraging dropout rate of only 20%, it was possible that these were motivated participants. There may be concern about whether the intervention can cause 'addiction' to computer games. This will not be likely considering that the training activities demand a sustained level of concentration which will limit the amount of time an individual can spend at one setting.

Compared to normal children, children with ADHD may have elevated relative theta power, reduced relative alpha and beta, together with elevated theta/alpha and theta/beta ratios.²⁰ Differences in brain electrical rhythms also exist between different ADHD subtypes.²¹ Based on the *hypothesis that training to alter these EEG rhythms which reflect underlying neuropathology can improve clinical symptoms*, neurofeedback was explored in the treatment of ADHD. Several treatment protocols exist and were done by skilled therapists, with controlled studies showing positive response rates over 75%.²¹ However in these conventional neurofeedback systems, the subject performs via trial-and-error from feedback cues to produce the required electrical rhythm. The key drawback of neurofeedback is that although brain rhythms are correlated with attention, the feedback system cannot distinguish if attention itself would positively result in a certain change in measurable values, i.e. the connection between attention and neurofeedback training program may be neither direct nor explicit. In our BCI system, the game is played through direct attention control, which allows the subject to know explicitly that an action is produced as intended. In addition, there is no need for the subject to follow any cue on the screen; this has also been referred to as an asynchronous mode. With such a mode, users can start to play the game straightaway, without any prior learning or quantitative EEG analysis, which may be necessary for neurofeedback.

Our intervention may have a place as one of the several arms of therapy in a multi-modal treatment programme, especially to target the more troublesome and pervasive inattentive symptoms or for children whose parents who do not wish for their children to receive medication. The study results show that 10 sessions over a 5-week period is unlikely to be effective. Further well-designed controlled clinical trials will be needed to clarify the efficacy of our intervention and to investigate for an optimal treatment schedule, for example, the optimal number of therapy sessions for the initial treatment, and the role of 'booster' sessions for maintenance treatment.

CONCLUSION

Childhood ADHD is associated with negative outcome in later years. It is important to explore new therapy to complement existing

treatment modalities. The efficacy of our BCI-based intervention will be assessed in a larger follow-up clinical trial. ❖

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ABBREVIATIONS

ADHD (Attention Deficit Hyperactivity Disorder), **BCI** (Brain-Computer Interface), **EEG** (electroencephalogram), **DSM-IV** (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition), **DISC-IV** (Diagnostic Interview Schedule for Children Version IV), **SD** (Standard Deviation).

TRIAL NO.

National Healthcare Group Domain Specific Review Board (Singapore) A/07/472.

CONFLICTS OF INTEREST

Intellectual property for the device has been filed under the provisions of the respective institutions.

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