Neeuro

White Paper

A Brain-Computer Interface Brain Training Game “CogoLand” for Children with Attention Deficit Hyperactivity Disorder

Complementing conventional approaches for treating ADHD

20 September 2019

Children becoming increasingly distracted?

Lack of attention or focus?

Executive Summary

Attention Deficit Hyperactivity Disorder (ADHD) is a cognitive disorder that afflicts approximately 2-7% of children globally. There is no cure, however the symptoms can be managed therapeutically. Treatment involves pharmaceutical intervention with the prescription of medications, or with behavioural intervention - where a clinician advises the parent(s) on how to reach certain behavioural outcomes with the ADHD child.

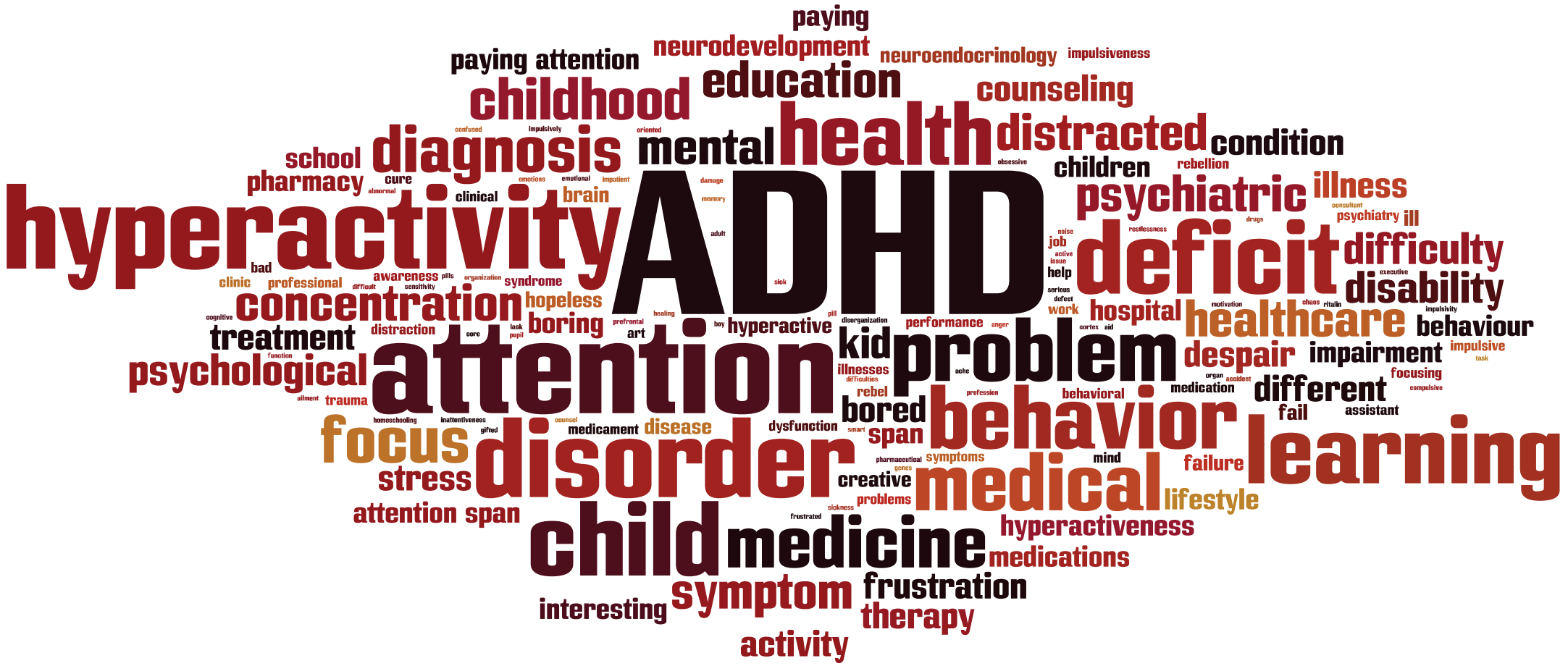
Prescription medications have the potential to cause addiction in the child and come with various side effects. Their dosages have to be carefully calibrated for maximum efficacy and minimal disruption of the child's function. Multiple appointments with the doctors are needed to tune requisite adjustments to the dosage. The efficacy of medication is short-term but also becomes less effective on the symptoms over time.

Behavioural therapy on the other hand is not as effective as medication but it is also much less invasive. Parents will need to make time for scheduling appointments with a therapist as well as, monitoring and following up on the behavioural outcomes of the child.

Clinical trials have proven that the use of neurofeedback with Brain-Computer-Interface (BCI) based games are effective at reducing the symptoms of ADHD, complementing current therapies by being non-invasive, conveniently digital and as such can be practiced with ease while avoiding the downsides being too much of a burden on time and monetary resources.

https://www.nuh.com.sg/ktp-nucmi/health/diseases-and-conditions/learning-and-behavioural-problems/attention-deficit-hyperactive-disorder-adhd.html

What is ADHD?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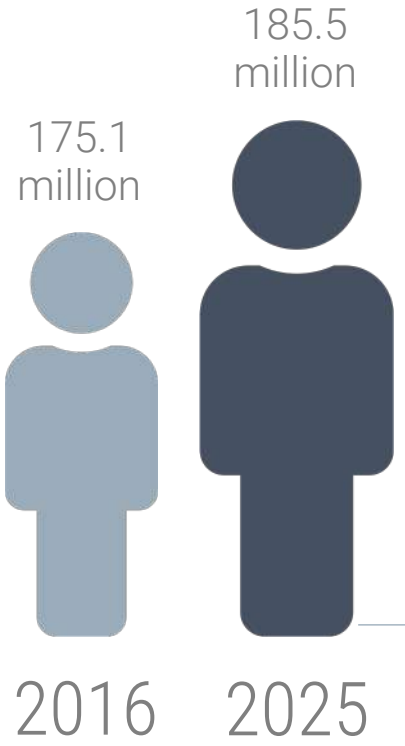
The Facts



Growing number of ADHD cases in people aged 5 to 44 years worldwide

Children with ADHD aged 5-19 years are estimated at 5.29%, while adults aged 20-44 years are estimated at 2.8%

https://www.businesswire.com/news/home/20180329005493/en/Market-Spotlight-Attention-Deficit-Hyperactivity-Disorder-ADHD

Current Treatments

Medications

They only treat the symptoms in the short term and need to be taken regularly in the long term. Without health insurance coverage, they can get expensive.

Medications also come with potentially significant side effects, that range from reduced appetite, headaches, sleep problems, reduced creativity, blunting of emotions and suicide ideation.

Behavior Therapy

Behavioural management, though important with some good results, has not been as effective as drugs in treating ADHD symptoms.

The treatments are effective only in the short-term as they lose effectiveness in the long-term due to compliance and sustainability. It can be very expensive as it requires consultations with clinicians.

Clinical Trials

Our therapeutic approach uses non-invasive BCI-based games to help children train themselves to learn to focus better.

This patented solution was developed from over 10 years of research with clinical trials by Singapore's Institute of Mental Health, Duke-NUS Medical School and A*STAR's Institute for Infocomm Research (I^2R).

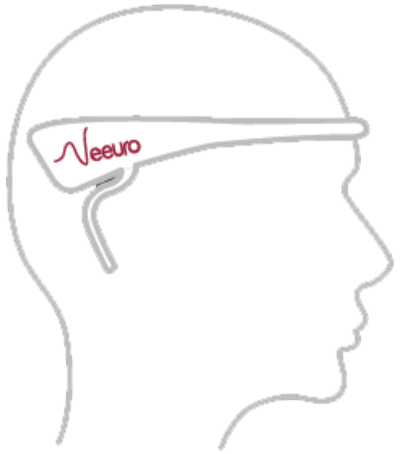
In the latest clinical trial that involved 172 ADHD children, it showed that children who received 8 weeks of intervention had significant improvements in their inattentive symptoms than those who did not receive any intervention, when rated by blinded clinicians.

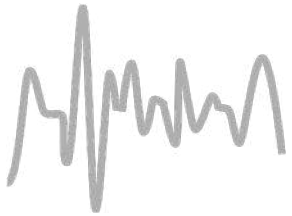
Additionally, through brain scans (fMRI), children in the intervention group showed reorganised brain network activity – increased closeness in prefrontal region of the brain that is associated with attention (i.e. less inattentive symptoms).

How It Works?

Machine learning algorithms on mobile applications interpret mental states in real-time, e.g. **attention**, **relaxation**, **mental workload** and **fatigue**; used to drive interventions for various brain challenges.

Brainwaves or EEG signals are captured passively through the Neeuro SenzeBand.



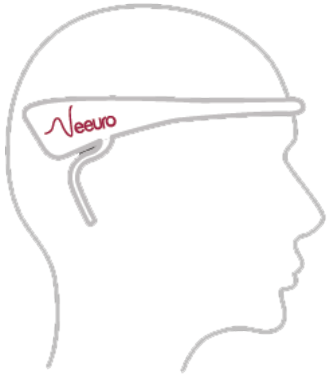


EEG Signals

Interventions are delivered through mobile applications that are Bluetooth paired with the SenzeBand.

Visual and audio stimuli through Neeuro's mobile applications provide positive reinforcement to the user.

Clinical Application - CogoLand



EEG Signals

The CogoLand game trains the user on attention and inhibition.

Attention level of the user computed from his/her EEG signals drives the virtual character on the screen to run faster.

This real-time visual feedback of the running virtual character motivates the user in learning how to focus.

The Journey

Pilot Study

Investigated on 10 unmedicated ADHD children, treated with 20 sessions over 10 weeks across 2 groups: intervention versus control.

The intervention group showed greater improvement in attentive scores on the ADHD Rating Scale (ADHD RS) as reported by parents and teachers, compared to the control group without intervention.

2010

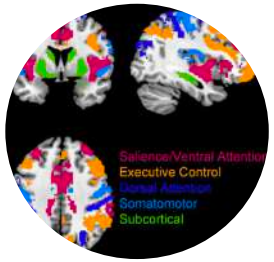
2012

Phase 1

Investigated a more intensive BCI-based attention training game system on 20 unmedicated ADHD children.

System was calibrated for each user individually with a treatment regime of an 8-week training comprising 24 sessions followed by 3 once monthly booster training sessions.

At week 8, the mean improvement was 26% and 30% for inattention and hyperactive impulsive symptoms respectively with a large effect size for inattentive symptoms at 0.78 on week 8.



Phase 2 - Brain Imaging Study

66 boys with ADHD went through the BCI-based game intervention for 24 sessions over 8 weeks. Assessments and brain scans (fMRI) were obtained at baseline and after 8 weeks.

The intervention group showed reorganised brain network activity – increased closeness in prefrontal region of the brain that is associated with attention (i.e. less inattentive symptoms).

2018

2019

Phase 2

Randomised control trial (RCT) conducted for 172 children aged 6 to 12 attending an outpatient child psychiatry clinic diagnosed with ADHD and not receiving concurrent pharmacotherapy or behavioural intervention.

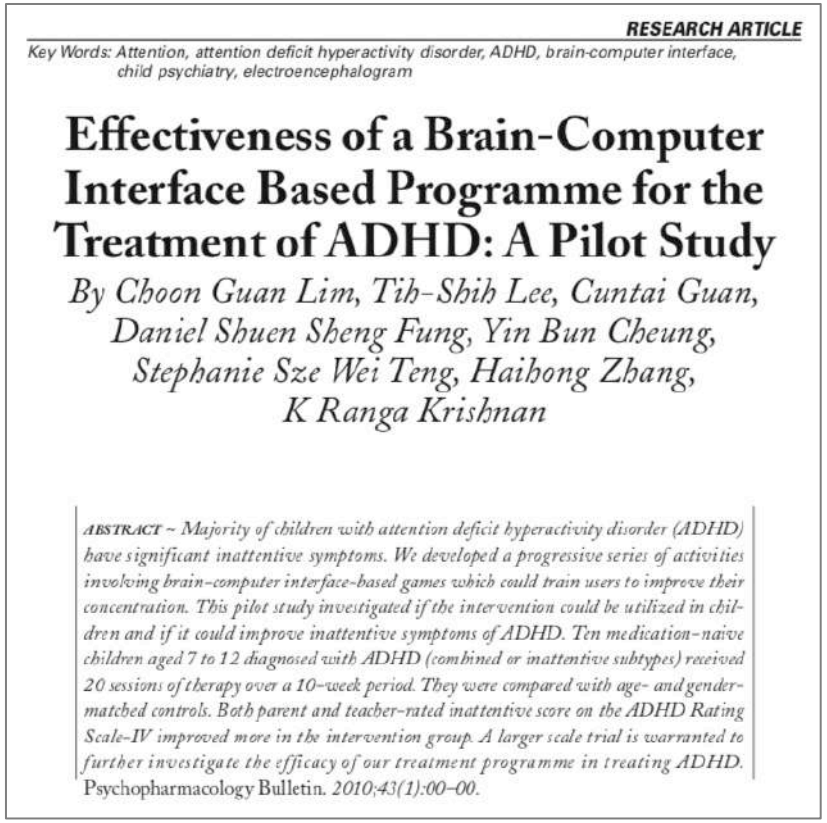
It showed children who received 8 weeks of intervention had significant improvements in their inattentive symptoms than those who did not receive any intervention, when rated by blinded clinicians.

Neeuro Licensed and Commercialised

Licensed the background technology and commercialised into a home-based kit with the Neeuro SenzeBand, incorporating enterprise features for tracking and monitoring.

Parents and children are able to carry on with their focus training in the convenience of their home.

Clinical Trial – Pilot Study



RESEARCH ARTICLE

Key Words: Attention, attention deficit hyperactivity disorder, ADHD, brain-computer interface, child psychiatry, electroencephalogram

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

By Choon Guan Lim, Tih-Shih Lee, Cuntai Guan, Daniel Shuen Sheng Fung, Yin Bun Cheung, Stephanie Sze Wei Teng, Haihong Zhang, K Ranga Krishnan

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-naive 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.*

In this study, the BCI-based attention brain training game system was investigated on 10 unmedicated ADHD children aged between 7 to 12 years old with inattentive and combined subtype symptoms.

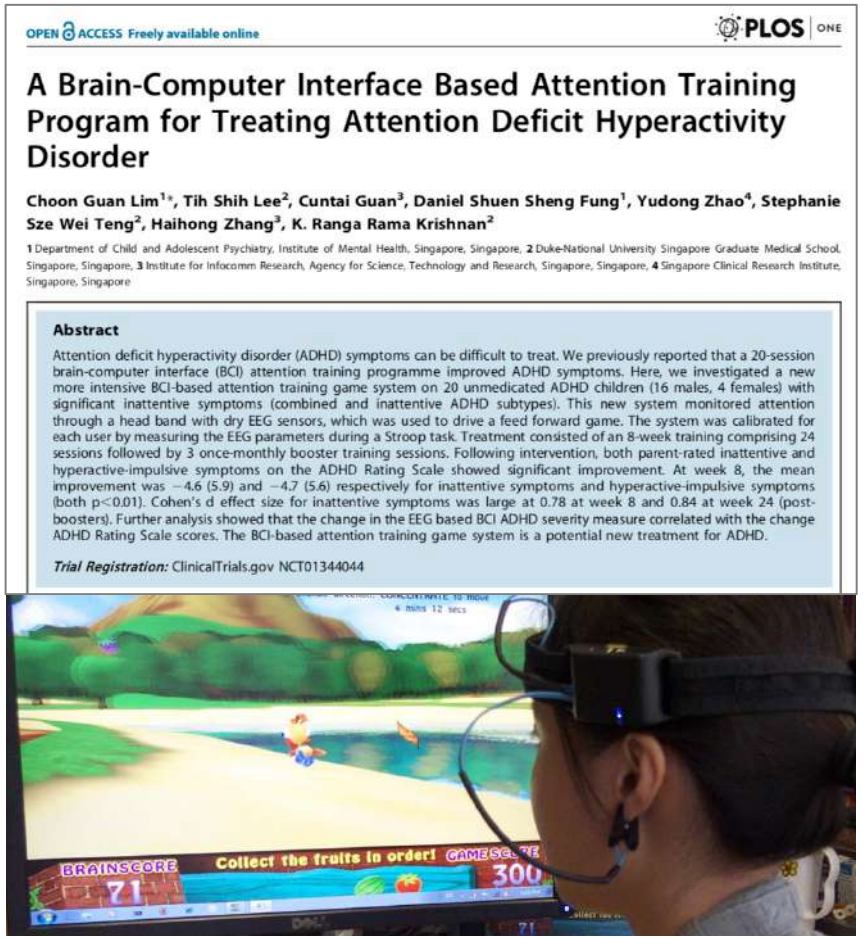
Treatment consisted 20 sessions over 10 weeks across 2 groups: intervention versus control.

The intervention group showed greater improvement in attentive scores on the ADHD Rating Scale (ADHD RS) as reported by parents and teachers, compared to the control group without intervention.

Reported by Parents:		Reported by Teachers:	
Intervention Group	% Improv.	Intervention Group	% Improv.
ADHD RS Inattention Score	16%	ADHD RS Inattention Score	36%
ADHD RS Hyperactive Score	23.5%	ADHD RS Hyperactive Score	33%
Control Group		Control Group	
ADHD RS Inattentive Score	-4%	ADHD RS Inattentive Score	6.5%
ADHD RS Hyperactive Score	11.4%	ADHD RS Hyperactive Score	30%

https://www.ncbi.nlm.nih.gov/pubmed/20581801

Clinical Trial – Phase 1 Study



OPEN ACCESS Freely available online

PLOS ONE

A Brain-Computer Interface Based Attention Training Program for Treating Attention Deficit Hyperactivity Disorder

Choon Guan Lim[1]*, Tih Shih Lee[2], Cuntai Guan[3], Daniel Shuen Sheng Fung[1], Yudong Zhao[4], Stephanie Sze Wei Teng[2], Haihong Zhang[3], K. Ranga Rama Krishnan[2]

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Abstract

Attention deficit hyperactivity disorder (ADHD) symptoms can be difficult to treat. We previously reported that a 20-session brain-computer interface (BCI) attention training programme improved ADHD symptoms. Here, we investigated a new more intensive BCI-based attention training game system on 20 unmedicated ADHD children (16 males, 4 females) with significant inattentive symptoms (combined and inattentive ADHD subtypes). This new system monitored attention through a head band with dry EEG sensors, which was used to drive a feed forward game. The system was calibrated for each user by measuring the EEG parameters during a Stroop task. Treatment consisted of an 8-week training comprising 24 sessions followed by 3 once-monthly booster training sessions. Following intervention, both parent-rated inattentive and hyperactive-impulsive symptoms on the ADHD Rating Scale showed significant improvement. At week 8, the mean improvement was −4.6 (5.9) and −4.7 (5.6) respectively for inattentive symptoms and hyperactive-impulsive symptoms (both $p<0.01$). Cohen's d effect size for inattentive symptoms was large at 0.78 at week 8 and 0.84 at week 24 (post-boosters). Further analysis showed that the change in the EEG based BCI ADHD severity measure correlated with the change ADHD Rating Scale scores. The BCI-based attention training game system is a potential new treatment for ADHD.

Trial Registration: ClinicalTrials.gov NCT01344044

In this study, the BCI-based attention brain training game system was investigated on 20 unmedicated ADHD children aged between 6 to 12 years old with inattentive and combined subtype symptoms.

The treatment consisted of 24 sessions of training over 8 weeks followed by 3 once-monthly booster training sessions with only an intervention group.

Following the completion of the intervention, parents-rated ADHD rating scale showed significant improvements in inattentive symptoms and hyperactive-impulsive symptoms.

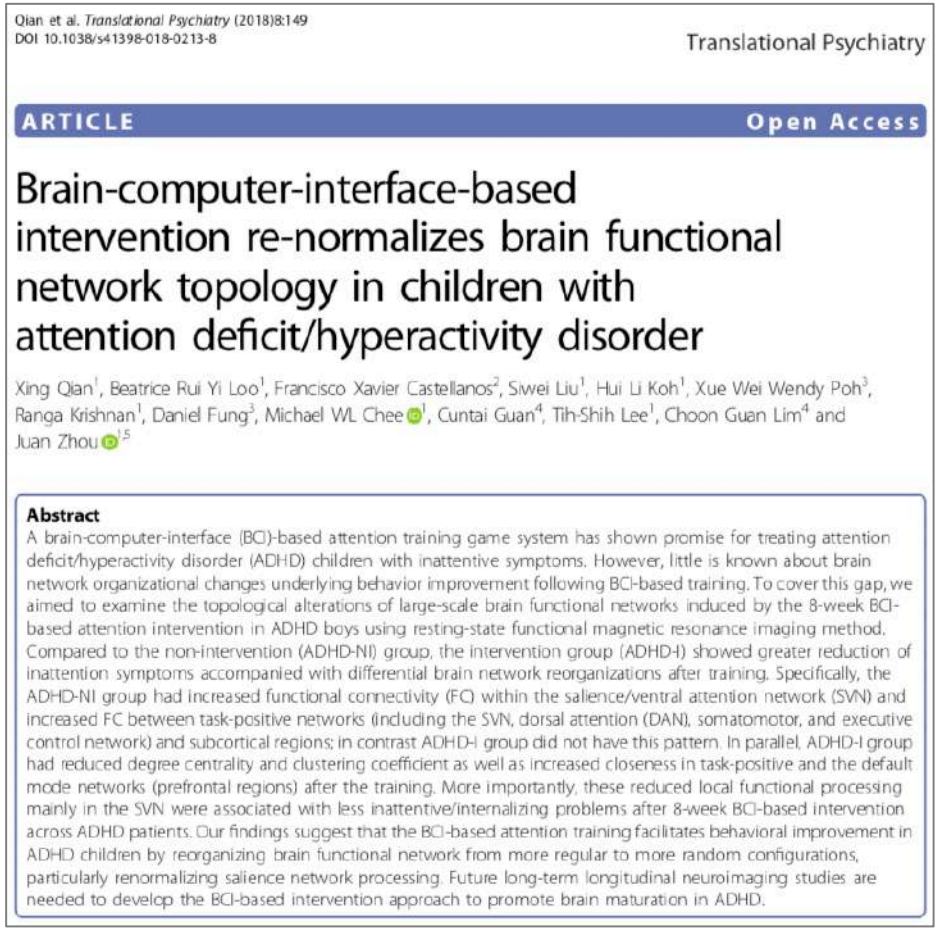
Better brain scores reflected in the training game was associated with lower ADHD symptoms reported by parents.

The results suggest that the additional 3 booster sessions did not improve the symptoms further.

Reported by Parents:	% Improv.
ADHD RS Inattention Score	26%
ADHD RS Hyperactive Score	30%
After Booster Sessions:	
ADHD RS Inattentive Score	-4%
ADHD RS Hyperactive Score	6.4%

https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0046692

Clinical Trial – Phase 2 Brain Imaging Study



Qian et al. *Translational Psychiatry* (2018)8:149
DOI 10.1038/s41398-018-0213-8

Translational Psychiatry

ARTICLE Open Access

Brain-computer-interface-based intervention re-normalizes brain functional network topology in children with attention deficit/hyperactivity disorder

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Abstract

A brain-computer-interface (BCI)-based attention training game system has shown promise for treating attention deficit/hyperactivity disorder (ADHD) children with inattentive symptoms. However, little is known about brain network organizational changes underlying behavior improvement following BCI-based training. To cover this gap, we aimed to examine the topological alterations of large-scale brain functional networks induced by the 8-week BCI-based attention intervention in ADHD boys using resting-state functional magnetic resonance imaging method. Compared to the non-intervention (ADHD-NI) group, the intervention group (ADHD-I) showed greater reduction of inattention symptoms accompanied with differential brain network reorganizations after training. Specifically, the ADHD-NI group had increased functional connectivity (FC) within the salience/ventral attention network (SVN) and increased FC between task-positive networks (including the SVN, dorsal attention (DAN), somatomotor, and executive control network) and subcortical regions; in contrast ADHD-I group did not have this pattern. In parallel, ADHD-I group had reduced degree centrality and clustering coefficient as well as increased closeness in task-positive and the default mode networks (prefrontal regions) after the training. More importantly, these reduced local functional processing mainly in the SVN were associated with less inattentive/internalizing problems after 8-week BCI-based intervention across ADHD patients. Our findings suggest that the BCI-based attention training facilitates behavioral improvement in ADHD children by reorganizing brain functional network from more regular to more random configurations, particularly renormalizing salience network processing. Future long-term longitudinal neuroimaging studies are needed to develop the BCI-based intervention approach to promote brain maturation in ADHD.

This neuroimaging study that is part of a larger randomised controlled study consisting of 172 children with ADHD. This study consisted of 66 boys with ADHD with symptoms of inattentive and combined subtype that went through the BCI based game intervention for 24 sessions over 8 weeks and they were split between intervention and non-intervention groups.

Assessments and brain scans (fMRI) were obtained at baseline and after 8 weeks.

Different brain networking activity were observed in both groups. Children in the non-intervention group showed more wide spread connectivity between spatially separated brain regions (i.e. increased functional connectivity) which is associated with higher ADHD symptoms.

Children in the intervention group showed reorganised brain network activity – increased closeness in prefrontal region of the brain that is associated with attention (i.e. less inattentive symptoms).

In summary, more focused brain area is activated after BCI intervention as compared to very wide spread activation of multiple brain areas in children from the non-intervention group.

https://www.nature.com/articles/s41398-018-0213-8

Clinical Trial – Phase 2 Randomised Controlled Trial

PLOS ONE

RESEARCH ARTICLE

A randomized controlled trial of a brain-computer interface based attention training program for ADHD

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Data Availability Statement: All relevant data are within the manuscript and its Supporting Information files.

Abstract

Objective

The use of brain-computer interface in neurofeedback therapy for attention deficit hyperactivity disorder (ADHD) is a relatively new approach. We conducted a randomized controlled trial (RCT) to determine whether an 8-week brain computer interface (BCI)-based attention training program improved inattentive symptoms in children with ADHD compared to a wait-list-control group, and the effects of a subsequent 12-week lower-intensity training.

Study design

We randomized 172 children aged 6–12 attending an outpatient child psychiatry clinic diagnosed with inattentive or combined subtypes of ADHD and not receiving concurrent pharmacotherapy or behavioral intervention to either the intervention or waitlist-control group. Intervention involved 3 sessions of BCI-based training for 8 weeks, followed by 3 training sessions per month over the subsequent 12 weeks. The waitlist-control group received similar 20-week intervention after a wait-time of 8 weeks.

A randomised controlled trial (RCT) was conducted for 172 children aged 6 to 12 attending an outpatient child psychiatry clinic diagnosed with ADHD and not receiving concurrent pharmacotherapy or behavioural intervention.

The intervention involved 3 weekly sessions of BCI-based training for 8 weeks, followed by 3 training sessions per month over the subsequent 12 weeks.

The intervention group showed significant improvement in their inattentive symptoms based on clinician rated ADHD Rating Scale (ADHD RS) Inattention score.

Post 8-Week Training	Intervention (n = 81)	Control (n = 82)
Week 0	18.9	18.6
Week 8	15.5	16.7
Change*	3.5	1.9

** Positive change scores indicate improvement from initial time-point*

Results suggests that this intervention is an option for treating milder cases or as an adjunctive treatment.

https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0216225

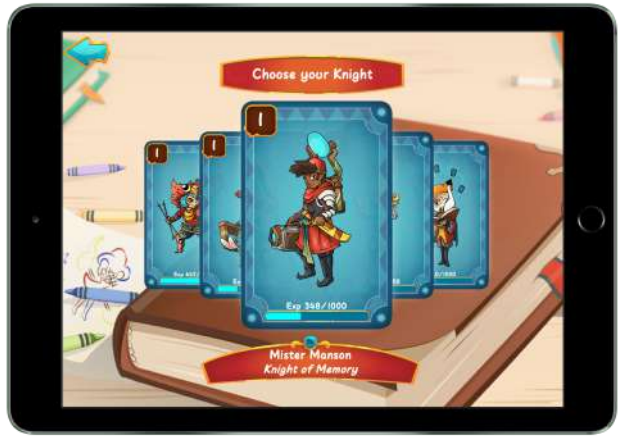
https://www.clinicaltrials.gov/ct2/show/NCT01344044?term=NCT01344044&rank=1

Making the Technology Available for the Masses

Having invested over 10 years of research and development, including clinical trials, the available evidence with BCI brain training with ADHD children showed that those who received 8 weeks of intervention had significant improvements in their inattentive symptoms compared to those that did not.

The BCI-based brain training game “CogoLand” used in clinical studies will soon be made available to children with ADHD.

Today, Neeuro has adapted the BCI technology used in “CogoLand” making it available for children to seniors seeking brain training to improve their cognitive functions, through its solution “Memorie” and “Smarty Knights”. These are paired with the Neeuro “SenzeBand” EEG headband. They provide BCI-based brain training in the 5 pillars of cognitive functions: (a) attention, (b) memory, (c) spatial ability, (d) decision making and (e) cognitive flexibility. Additionally, it includes educational content in English and Mathematics while providing real time feedback on attention levels.



Smarty Knights

Memorie

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