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A Brain-Computer Interface Based Treatment Programme for ADHD

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Dept of Developmental Psychiatry, IMH

A Member of the **National Healthcare Group**

Conflict of Interest

- IP filed under provisions of IMH, A*STAR, Duke-NUS
- Licensed to Neeuro
- No financial conflict

Highly prevalent 5%

Childhood onset, chronic course

- Inattentive (more persistent)
- Hyperactive-impulsive

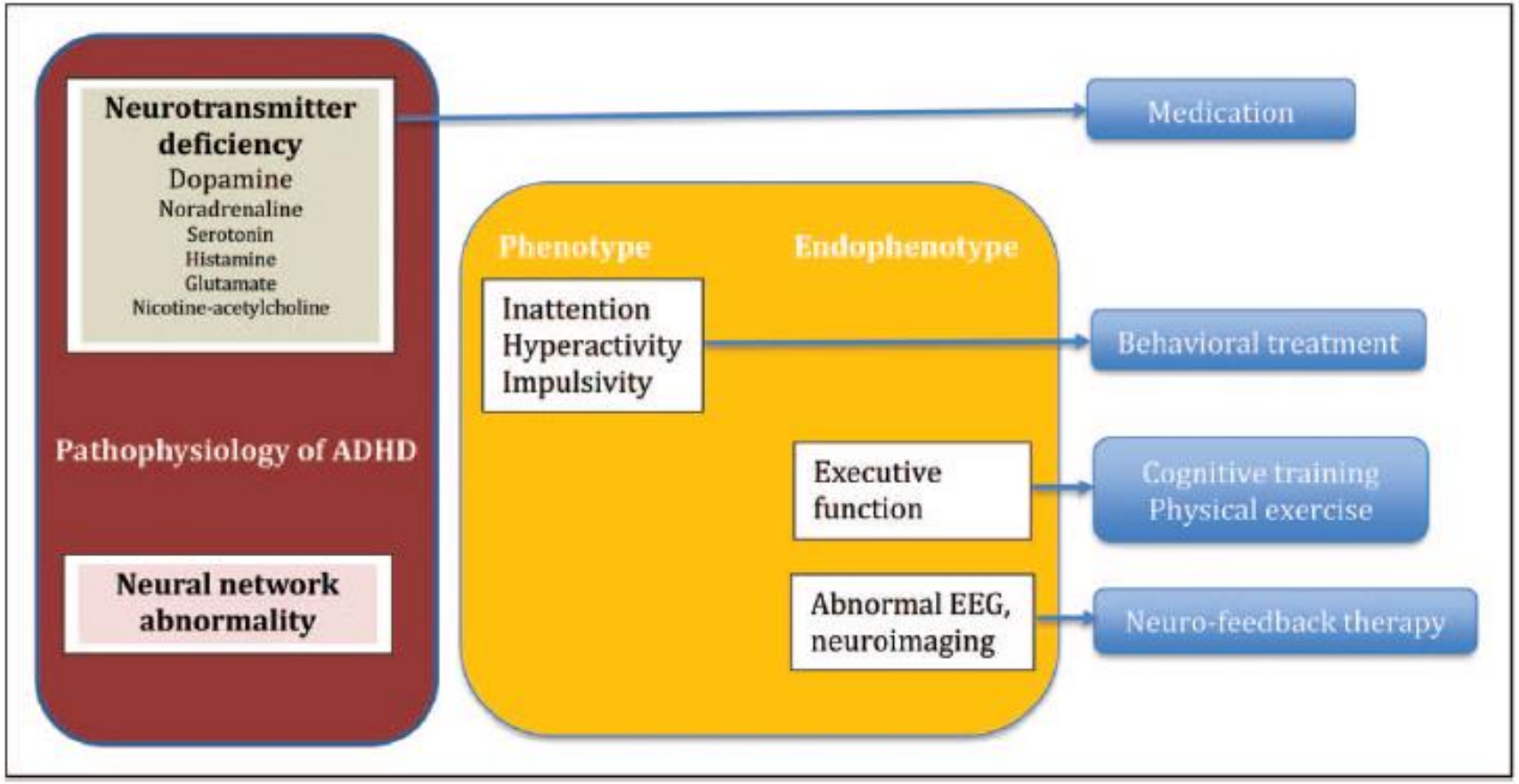
ADHD

Academic/occupational underachievement, motor accidents, relational problems

High burden

Treatment

- Present evidence-based treatment of ADHD
  - Pharmacological
    - Parents concerned about side effects
    - Doesn't teach the child skills
    - Controls symptoms but doesn't cure
  - Psychosocial treatment
    - Manpower intensive
    - Intensive, collaborative effort with school/family
    - Time to see results



Pathophysiology of attention deficit hyperactivity disorder and targets of intervention.

Lim CG, Lim-Ashworth NSJ, Fung DSS. Updates in technology-based interventions for ADHD. Current Opinion in Psychiatry. 2020 Nov.

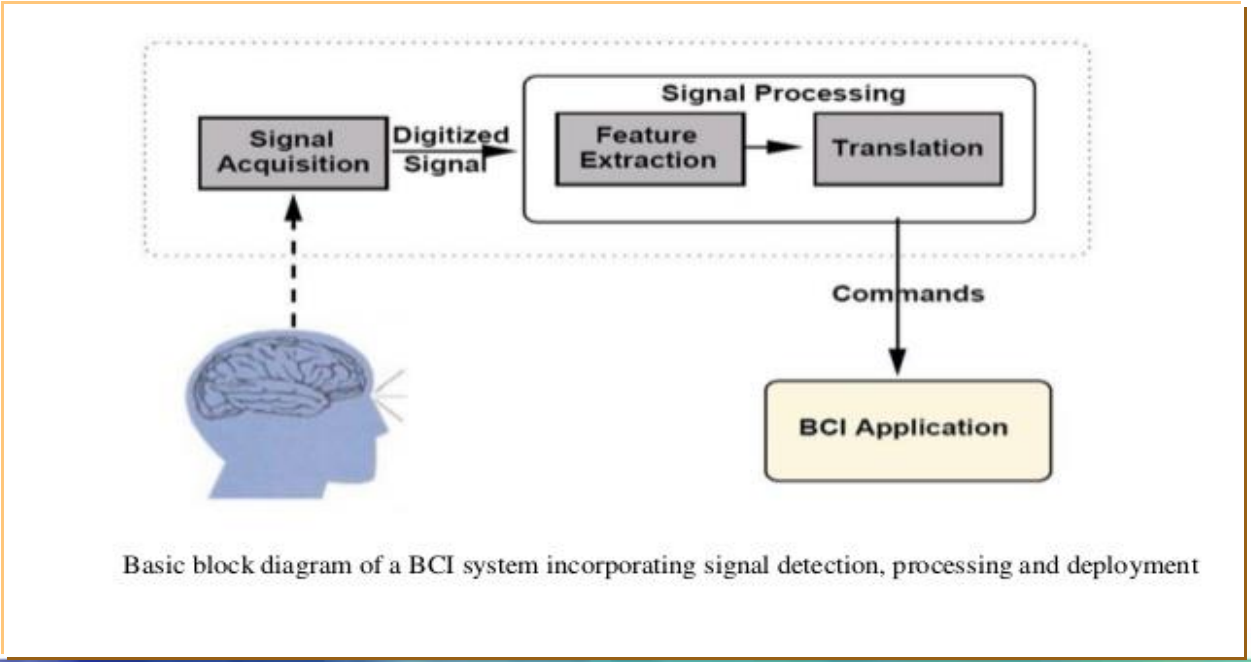
EEG Abnormalities in ADHD

- Increased relative slow wave activity
  - Theta activity (frontal)
  - Delta (posterior)
- Decreased relative alpha and beta activity (posterior)
- Increased theta-beta ratio
- Development of neurofeedback therapy

Clarke AR, et al. An Investigation of Stimulant Effects on the EEG of Children With ADHD. Clin EEG Neurosci. 2016 Aug 23. pii: 1550059416664657

What Is BCI?

- Direct communication pathway between brain and external device.
- EEG: most studied non-invasive interface



Basic block diagram of a BCI system incorporating signal detection, processing and deployment

BCI Attention System

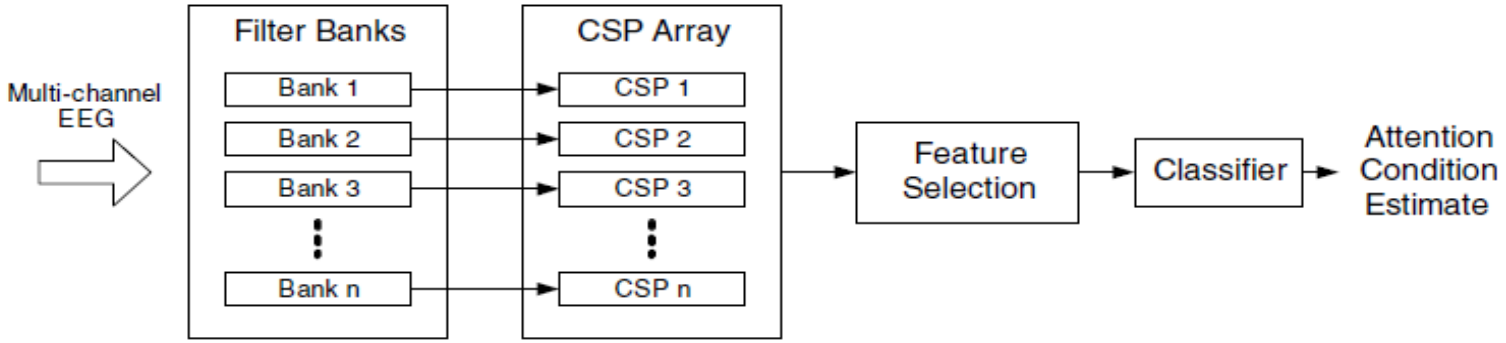


Fig. 1. Schematic flowchart of attention monitoring

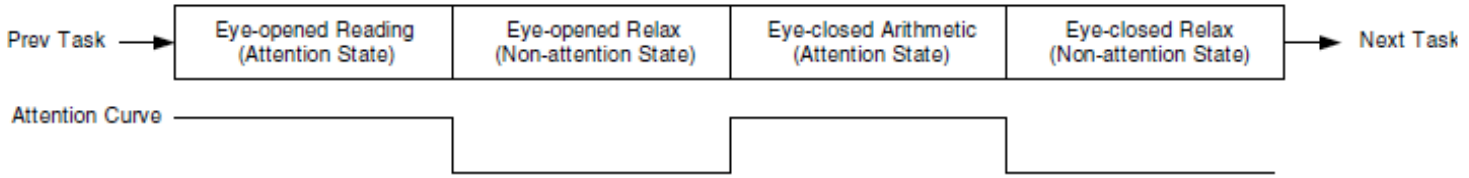
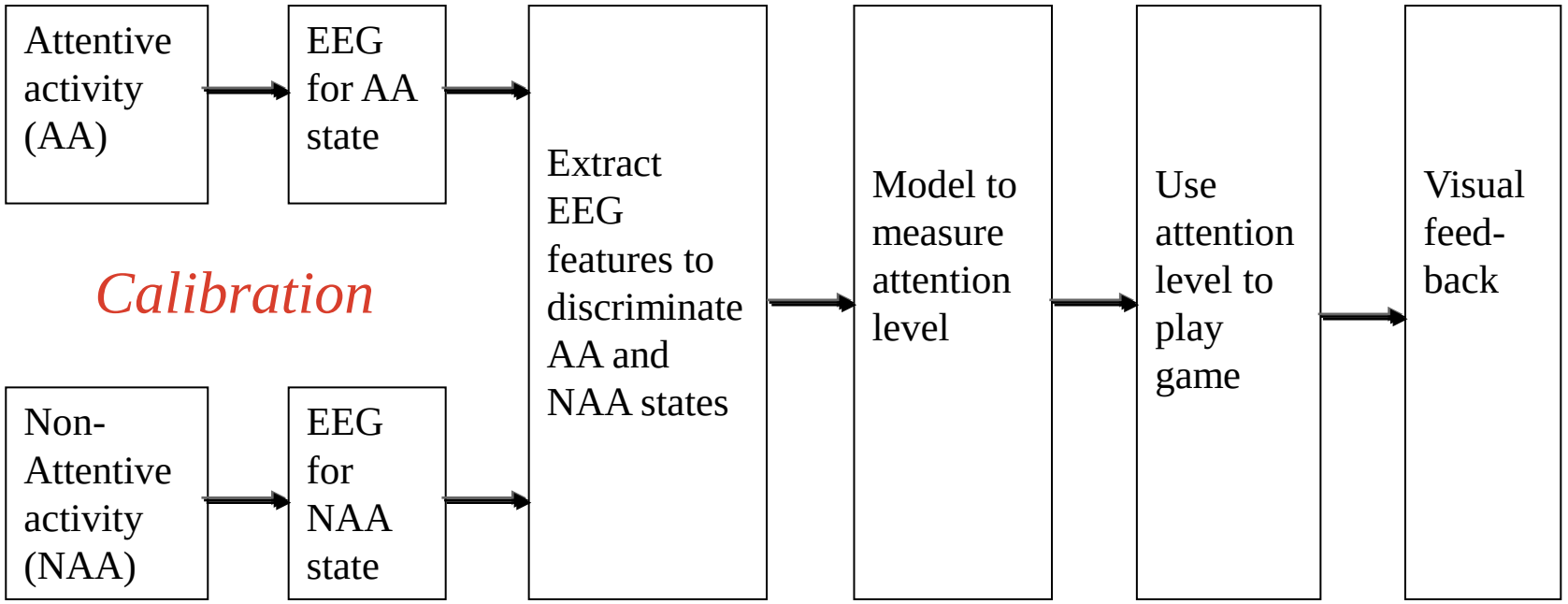


Fig. 2. Sequence of attention / non-attention tasks during one run

Hamadicharef B, Zhang HH, Guan CT, Wang CC, Phua KS, Tee KP, et al, Learning EEG-Based Spectral-Spatial Patterns for Attention Level Measurement. In proceedings of the IEEE International Symposium on Circuits and Systems (ISCAS) May 24-27, 2009, Taiwan, pp1465-8.

The BCI System

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Study 1

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

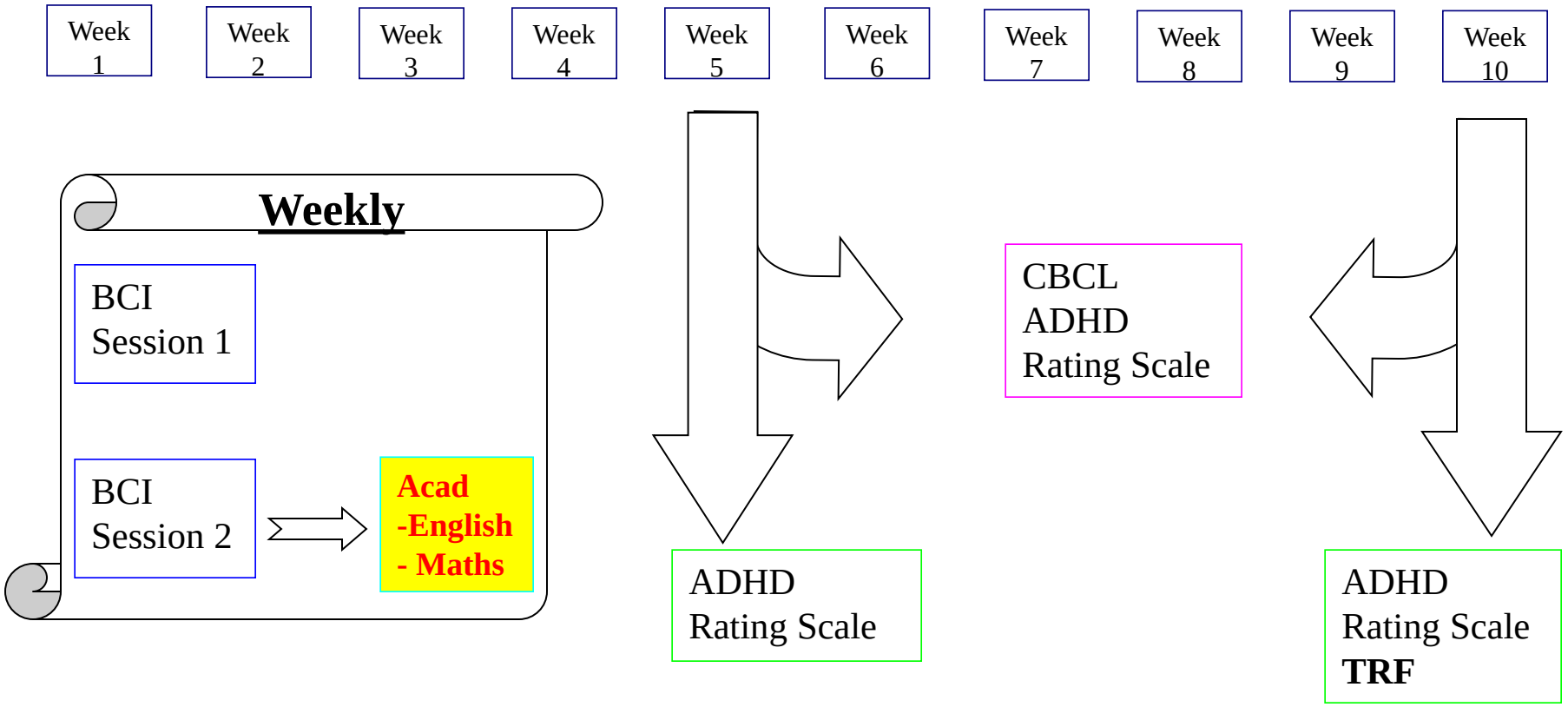
By Choon Guan Lim, Tih-Shih Lee, Cuntai Guan, Daniel Shuen Sheng Fung, Yin Bun Cheung, Stephanie Sze Wei Teng, Haihong Zhang, K Ranga Krishnan

Psychopharmacology Bulletin. 2010;43(1):73-82.

Methodology

- 10 pairs of children aged 7-12 with ADHD, never medicated
- 16 males: 4 females
- Intervention (2x/wk 10 wks) vs control
- Diagnosis of ADHD, Combined or Inattentive subtype, based on C-DISC

Intervention Group



Mean Attention Score Change in ADHD Rating Scale (parent) Wk 0-10

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)

Mean Attention Score Change in ADHD Rating Scale (teachers) Wk 0-10

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)

Study 2

OPEN ACCESS Freely available online

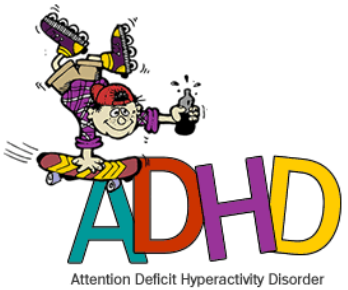
PLOS ONE

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]

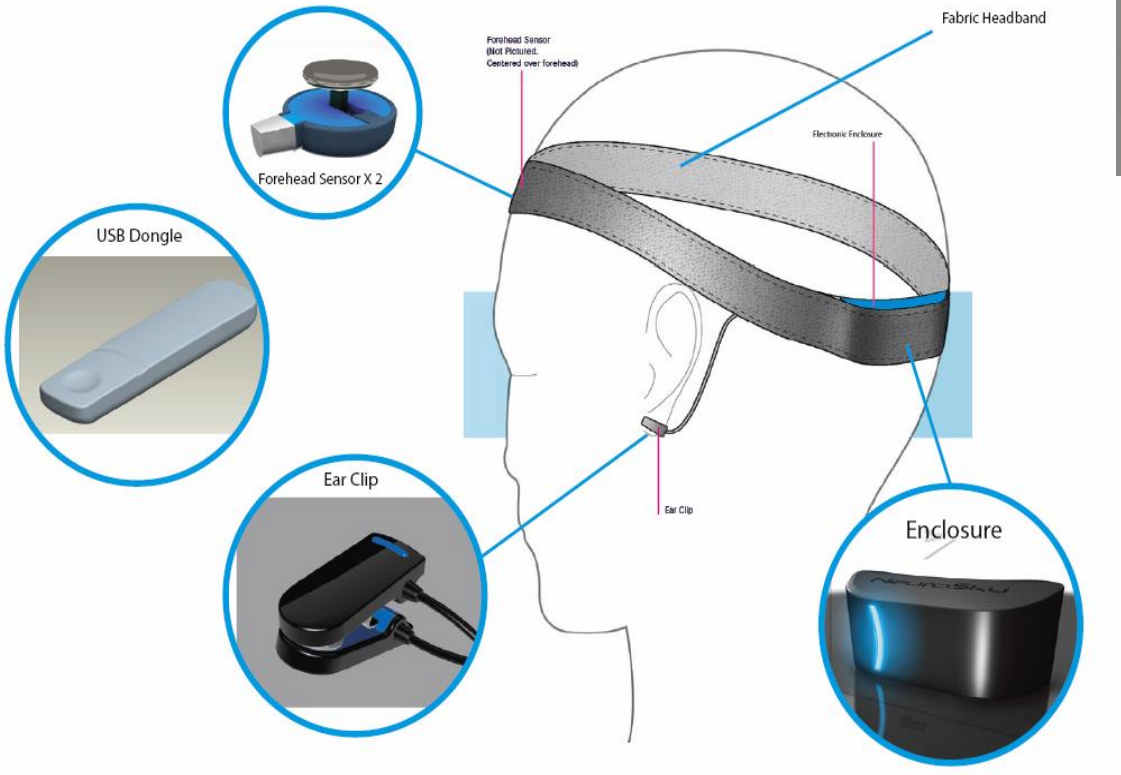
1 Department of Child and Adolescent Psychiatry, Institute of Mental Health, Singapore, Singapore, **2** Duke-National University Singapore Graduate Medical School, Singapore, Singapore, **3** Institute for Infocomm Research, Agency for Science, Technology and Research, Singapore, Singapore, **4** Singapore Clinical Research Institute, Singapore, Singapore

PLOS One. 2012 Oct 24;7:10;e46692



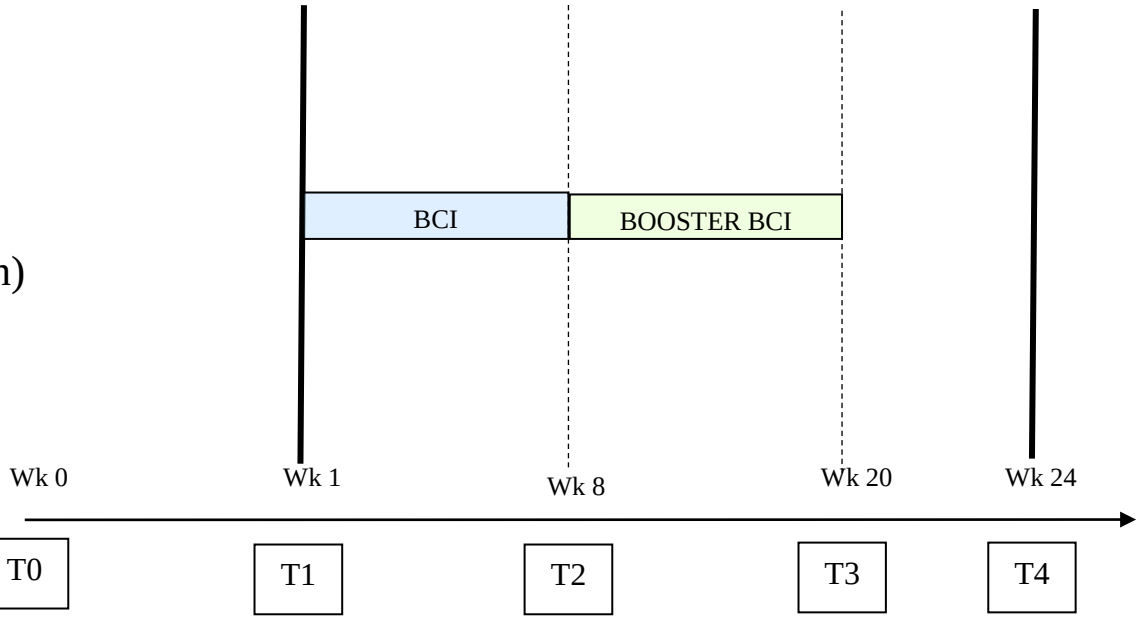
New Game ‘Cogoland®’

Dry Sensors


Fabric Headband
Forehead Sensor
(Not Pictured.
Centered over forehead)
Electronic Enclosure
Forehead Sensor X 2
USB Dongle
Ear Clip
Ear Clip
Enclosure

Study Design

(*n* = 20)
- BCI (3x/wk)
- Boosters (1x / month)



Questionnaires and Assessments for Phase 1

Pre-screening
CDISC

Child:
K-BIT2 (selected)

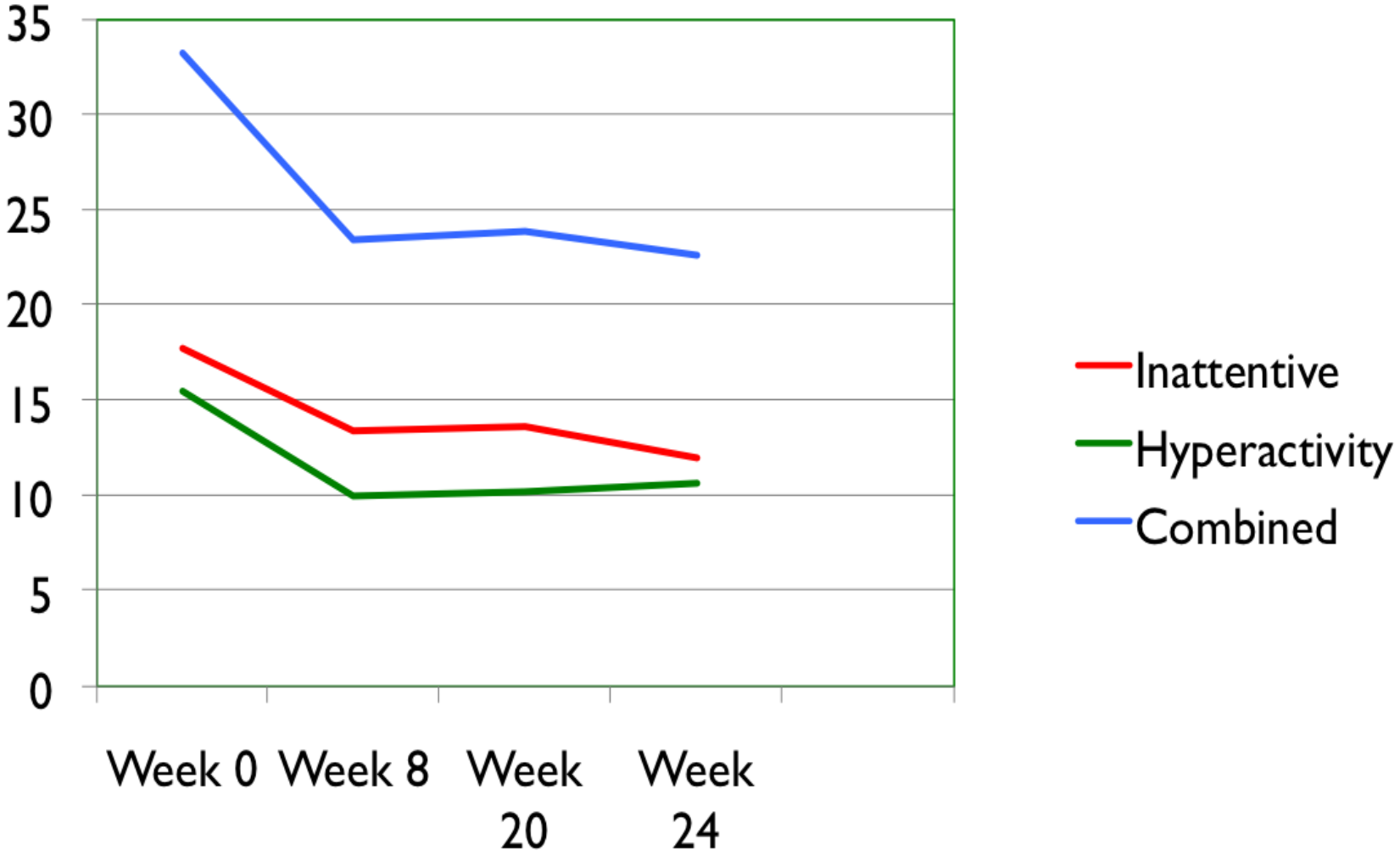
Baseline
Teacher :
ADHD-RS / TRF
Parents:
ADHD-RS / CBCL
Clinician:
C-GAS / CGI / PAERS
Child:
WIAT-III
CPT

Post-Tx
Teacher :
ADHD-RS / TRF
Parents:
ADHD-RS / CBCL
Clinician:
C-GAS / CGI / PAERS
Child:
CPT

Post-Boosters
Teacher :
ADHD-RS / TRF
Parents:
ADHD-RS / CBCL
Clinician:
C-GAS / CGI / PAERS

1-mth follow-up
Teacher :
ADHD-RS / TRF
Parents:
ADHD-RS / CBCL
Clinician:
C-GAS / CGI / PAERS
Child:
WIAT-III
CPT

Clinician Rating



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RCT

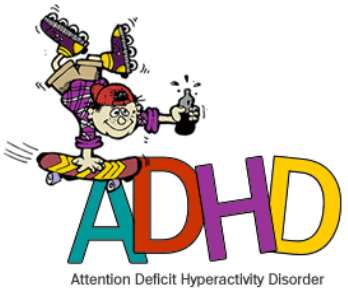
PLOS ONE

RESEARCH ARTICLE

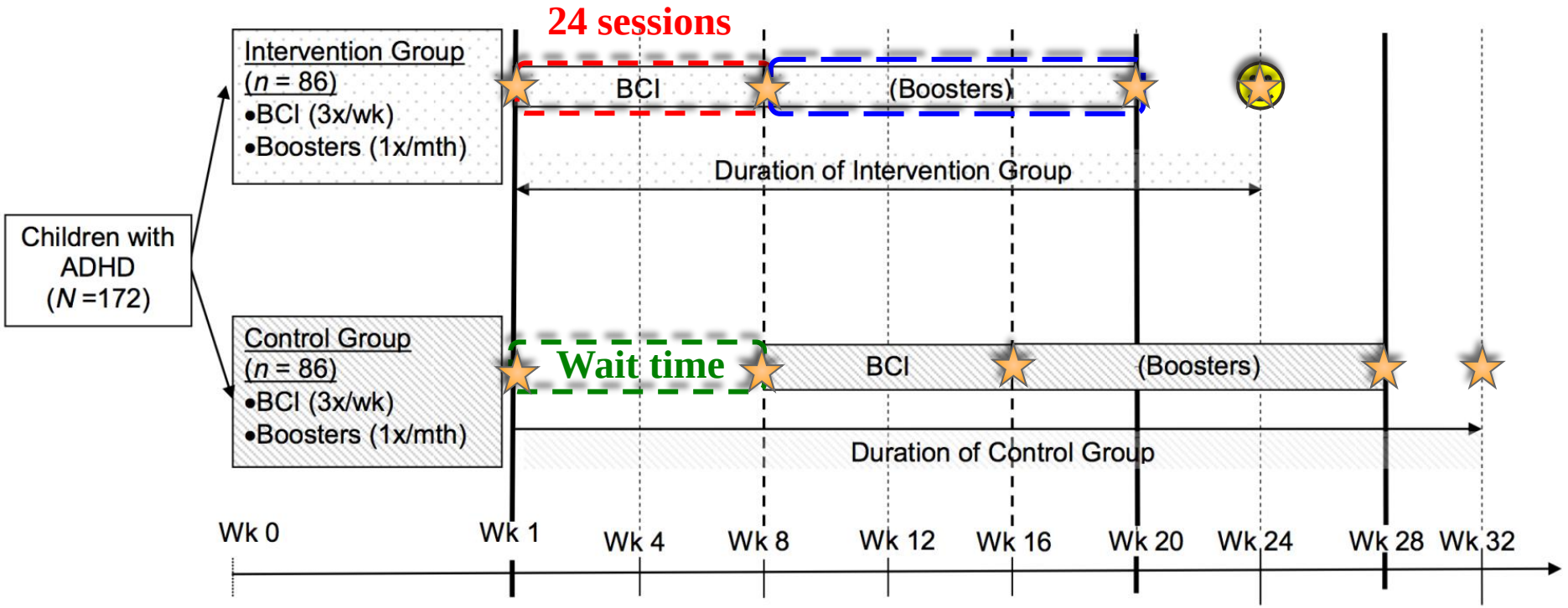
A randomized controlled trial of a brain-computer interface based attention training program for ADHD

Choon Guan Lim[1]*, Xue Wei Wendy Poh[1], Shuen Sheng Daniel Fung[1], Cuntai Guan[2], Dianne Bautista[3,4], Yin Bun Cheung[3,4,5], Haihong Zhang[6], Si Ning Yeo[7], Ranga Krishnan[7], Tih Shih Lee[7]

PLOS ONE | https://doi.org/10.1371/journal.pone.0216225 May 21, 2019



Randomized Controlled Trial



Primary Outcome **ADHD-RS** **ADHD-RS**
(Clinician-rated)

RCT: Study Groups

	Intervention (N = 81)	Waitlist Control (N = 82)	Total (N = 163)
Age (years)			
n	81	82	163
Mean (SD)	8.7 (1.37)	8.6 (1.69)	8.6 (1.54)
Median (IQR)	9.0 (2.00)	8.0 (3.00)	8.0 (2.00)
Min, Max	6.0 , 12.0	6.0 , 12.0	6.0 , 12.0
Gender			
Male	69 (85.2)	69 (84.1)	138 (84.7)
Female	12 (14.8)	13 (15.9)	25 (15.3)
Ethnicity			
Chinese	72 (88.9)	74 (90.2)	146 (89.6)
Malay	3 (3.7)	3 (3.7)	6 (3.7)
Indian	4 (4.9)	2 (2.4)	6 (3.7)
Others	2 (2.5)	3 (3.7)	5 (3.1)
Current education			
Primary	81 (100)	82 (100)	163 (100)

Our RCT: Primary Outcome

Time Point	BCI-Intervention (n=81)		Waitlist control (n=82)	
	Mean	SD	Mean	SD
Week 0	18.9	4.25	18.6	4.38
Week 8	15.5	4.48	16.7	5.14
Change*	3.5	3.87	1.9	4.42

Mean diff (95% CI)	1.59 (0.28, 2.89)
Effect size (95% CI)	0.38 (0.07, 0.70)
p-value**	0.0177

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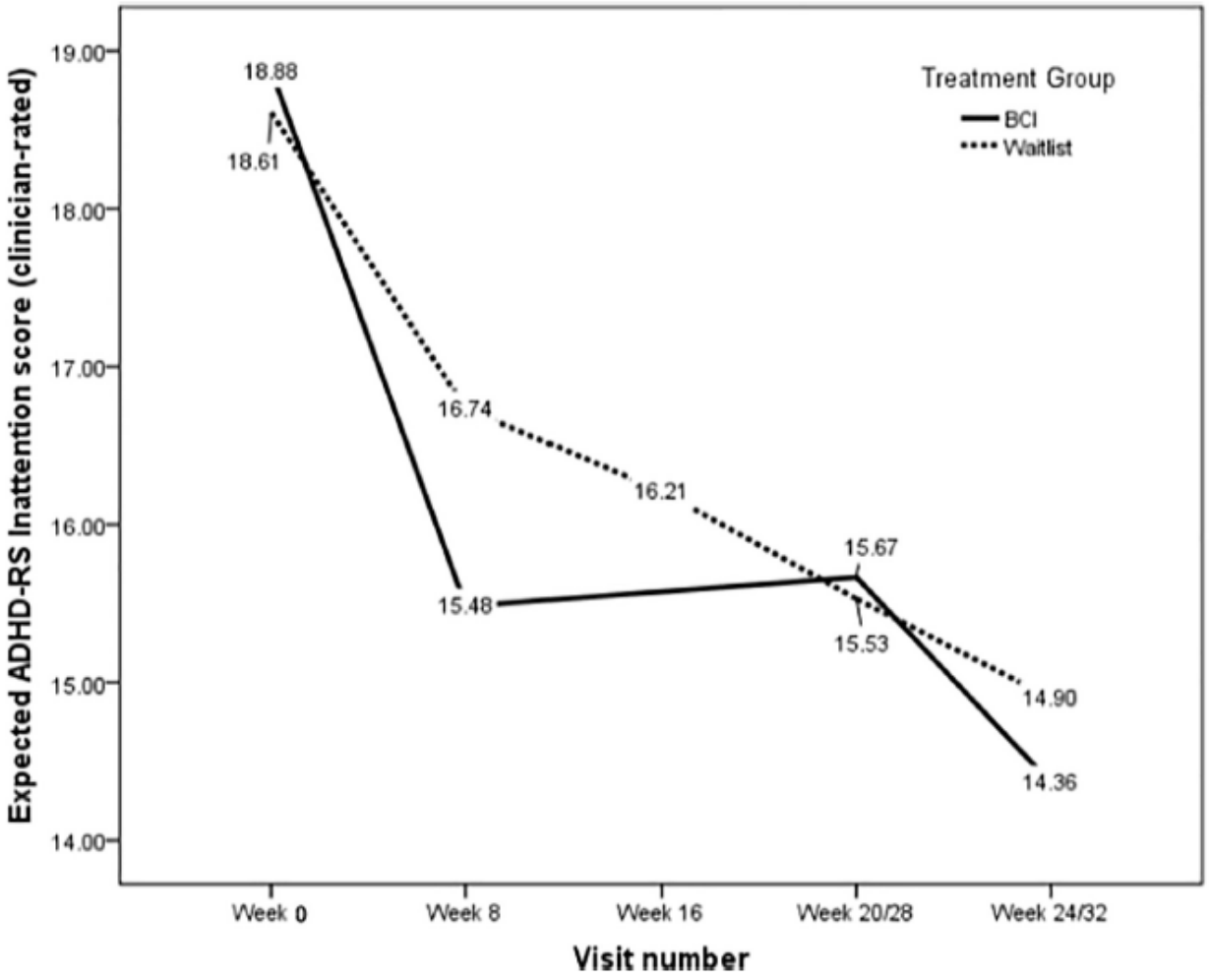
RCT: Results



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Neuroimaging 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

Xing Qian[1], Beatrice Rui Yi Loo[1], Francisco Xavier Castellanos[2], Siwei Liu[1], Hui Li Koh[1], Xue Wei Wendy Poh[3], Ranga Krishnan[1], Daniel Fung[3], Michael WL Chee[1], Cuntai Guan[4], Tih-Shih Lee[1], Choon Guan Lim[4] and Juan Zhou[1,5]

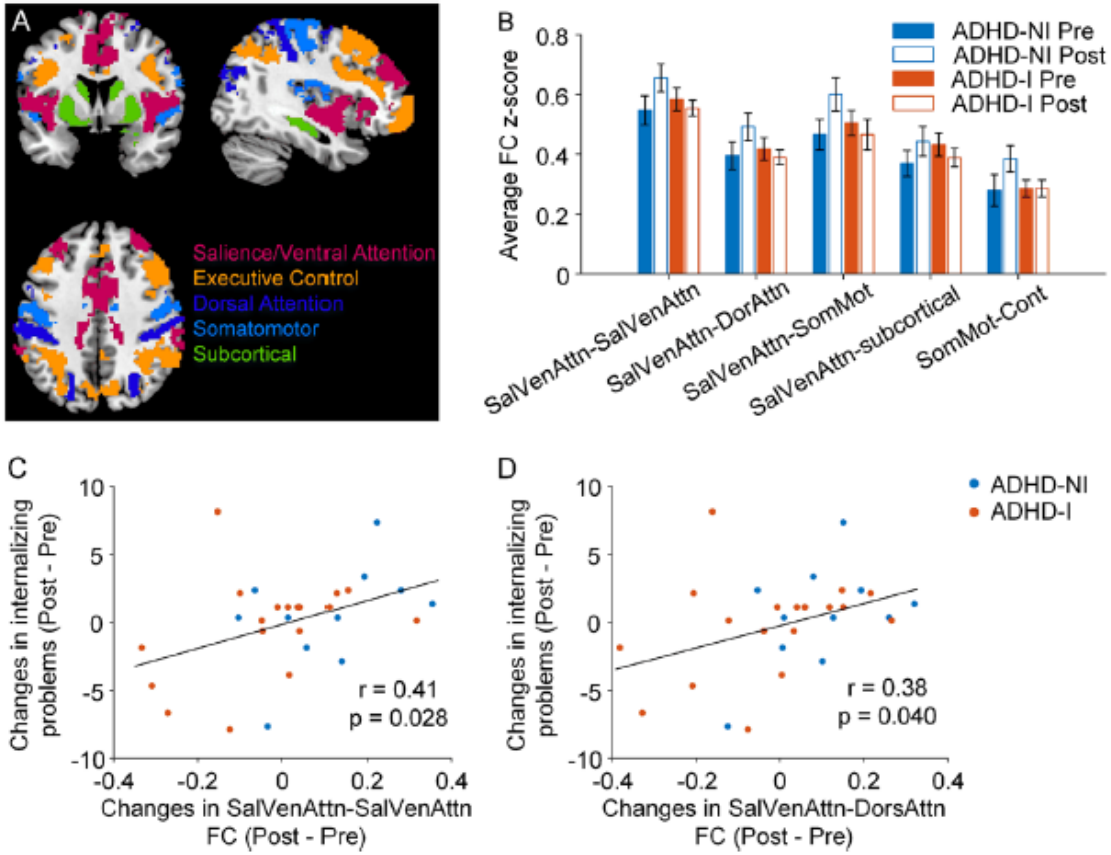
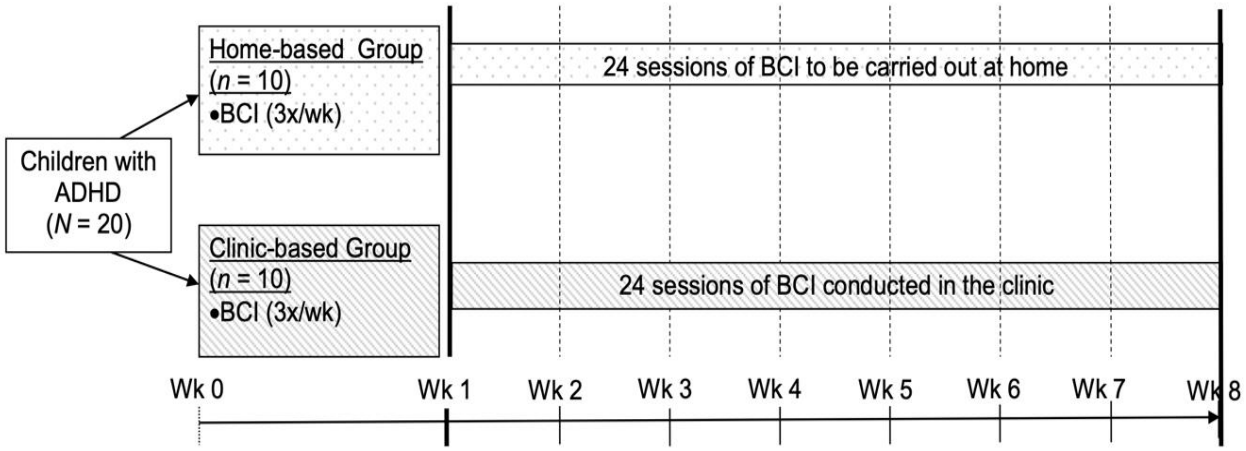


Fig. 3 Changes in intra- and inter-network functional connectivity (FC) of the attentional networks related to behavioral improvement in ADHD after the BCI-based intervention. a Brain slices highlight the major intrinsic connectivity networks and subcortical regions[38]. **b** Intra- and

Qian X, Loo BRY, Castellanos FX, Liu S, Koh HL, Poh XWW, Krishnan R, Fung D, Chee MWL, Guan CT, Lee TS, Lim CG, Zhou J., BCI-based intervention re-normalizes brain functional network topology in children with ADHD. Translational psychiatry. 2018; 8:149, 1-11.

Home-based therapy: can it work?

- N=20 (M_{age} = 9.93, SD = 1.69) recruited
  - 16 males (80%) and 4 females (20%)
  - Not on medication



Results: Feasibility

	Total	Home	Clinic
Completion and retention			
Treatment completion (at least 20 sessions)	95% (19/20)	95% (9/10)	95% (9/10)
Treatment completion (all 24 sessions)	90% (18/20)	95% (9/10)	95% (9/10)
Retention (post-intervention)	100% (20/20)	100% (10/10)	100% (10/10)
Session spread			
3 sessions/week throughout trial	15% (3/20)	30% (3/10)	0% (0/10)
More than 3 weeks of having 3 sessions/week	60% (12/20)	30% (3/10)	90% (9/10)
Technical issues			
Headband disconnectivity	30% (6/20)	30% (3/10)	30% (3/10)
Game application software hanging/crashing	0% (0/20)	0% (0/10)	0% (0/10)
Gameplay defect	0% (0/20)	0% (0/10)	0% (0/10)
Other difficulties			
Game set up by parents[a,b]	-	20% (2/10)	-
Game set up by child[a,b]	-	0% (0/10)	-
Require parent supervision[a,b]	-	20% (2/10)	-
Gameplay[b]	25% (5/20)	20% (2/10)	30% (3/10)
Adverse events			
Serious adverse events	0	0	0
Sleep problems	0	0	0
Somatic complaints	5% (1/20)	10% (1/10)	0
Other complaints[c]	5% (1/20)	0	10% (1/10)

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Clinical Ratings

	Home (Mean, SD)	Clinic (Mean, SD)	*U*	*z*	*p*	*r*
Clinician-rated Inattention score						
Week 0	17.9 (5.61)	16.1 (5.69)				
Week 8	14.7 (4.97)	14.0 (6.30)	42.0	0.179	.90	0.04
Change	-3.2[a] (6.20)	-3.9[a] (5.08)				
Parent-rated Inattention score						
Week 0	17.7 (4.32)	15.9 (6.97)				
Week 8	14.7 (4.97)	14.1 (6.31)	39.5	-0.798	.44	-0.19
Change	-3.0[a] (4.24)	-1.8[a] (4.39)				
Clinician-rated Hyperactivity score						
Week 0	12.5 (5.72)	10.9 (8.16)				
Week 8	11.2 (6.23)	10.3 (5.02)	46.0	0.541	.63	0.12
Change	-1.3[a] (4.17)	-2.5[a] (4.34)				
Parent-rated Hyperactivity score						
Week 0	12.2 (5.37)	11.8 (8.44)				
Week 8	11.4 (6.26)	9.7 (5.29)	60.5	0.804	.44	0.19
Change	-0.8[a] (3.74)	-2.1[a] (4.15)				

[a]Negative mean change scores indicate improvement in reported symptoms.

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Future Directions

- Optimal treatment schedule
- Other psychiatric conditions

Acknowledgement

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  - Prof Lee Tih-Shih
  - Dr Helen Zhou
  - Ms Stephanie Teng
- **NTU**
  - Dr Guan Cuntai
- **SCRI**
  - Prof Cheung Yin Gun
- **Ministry of Education**
- **Parents and children** who helped us!

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Thank You

A Member of the **National Healthcare Group**