Braingaze

Interactive Eye-tracking Games for Early Detection and Treatment of People with ADHD

Vision and Mission

Braingaze brings mental health care into the **digital**, **AI-empowered** age along with **digital biomarkers**, **digital therapy**, and practice-inspired patient journeys that are convenient and trustworthy.

Cognitive brain afflictions affect a large part of humanity, and are very often not detected on time

Attention Deficit and Hyperactivity Disorder (ADHD)

12 million diagnosed

Estimated 2-3% of population = 200 million people worldwide suffer from ADHD

Alzheimer's Disease (AD)

50 million diagnosed with AD

Estimated 6-7% of people over 60 are suffering from Mild Cognitive Impairment which in 60-70% of the cases develops into Alzheimer's disease within 3-5 years Braingaze exploits the connection between eye metrics (Cognitive Vergence) and ADHD & AD

Activity of Brainstem can be assessed by eye metrics



Brainstem is critical in ADHD and AD

- <u>Bast, N., et al (2018)</u> The locus coeruleus–norepinephrine system as pacemaker of attention a developmental mechanism of derailed attentional function in autism spectrum disorder Eur J Neurosci, 47: 115-125.
- <u>D'Andrea, I., et al. (2015)</u>.Lack of kinase-independent activity of PI3Kγ in locus coeruleus induces ADHD symptoms through increased CREB signaling. EMBO molecular medicine, 7(7), 904–917. https://doi.org/10.15252/emmm.201404697
- <u>Mueller A et al.</u> (2017)Linking ADHD to the Neural Circuitry of Attention Trends Cogn Sci. 21(6): 474–488.
- <u>Murphy PR, et al.</u> Pupil diameter covaries with BOLD activity in human locus coeruleus. Hum Brain Mapp. 2014;35:4140–4154.
- <u>Siddhartha J et al., (2016)</u> Relationships between Pupil Diameter and Neuronal Activity in the Locus Coeruleus, Colliculi, and Cingulate Cortex Neuron 89:221-234.
 https://doi.org/10.1016/j.neuron.2015.11.028
- https://doi.org/10.1016/j.neuron.2015.11.028
- Sparks, D. (2002) The brainstem control of saccadic eye movements. Nat Rev Neurosci 3, 952–964. https://doi.org/10.1038/nrn986

Cognitive Vergence; the core invention which permits us to measure cognitive functions by just analyzing involuntary eye movement patterns



- Vergence is movement of both eyes in opposite direction
- Novel role of vergence in cognitive processing
- This method is called Cognitive Vergence is patented worldwide by Braingaze

Role of Cognitive vergence in cognitive functions



Sole et al., PLOS One 2013a Sole et al., PLOS One 2013b Sole et al., PLOS One 2015 Jimenez et al., Vis Research 2020 Esposito & Supèr, Acta Psychologica 2019 Sole et al., submitted Sole et al., Neuroreport 2016 Esposito & Supèr, Neuroreport 2018 Jimenez et al., in prep

Cognitive vergence correlates with EEG responses



Sole et al., PLoS One 2016

The fundamental tech is patented worldwide

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Title

(EN) METHOD OF MEASURING ATTENTION (FR) PROCÉDÉ DE MESURE DE L'ATTENTION

Fig.1a

Abstract

(EN)

(FR)

In a first aspect, the present invention provides a method of measuring attention of a person comprising presenting one or more stimulus aimed at attracting attention of the person; and obtaining positions of the eyes of the person. The method further comprises detecting one or more eye fixations from the obtained positions of the eyes; and measuring the angle of convergence of the eyes or time from the obtained positions of the eyes during one or more or more of the detected eye fixations.

Dans un premier aspect, la présente invention concerne un procédé de mesure de l'attention d'une personne, comprenant la présentation d'un ou de plusieurs stimuli visant à attirer l'attention de la personne ; et l'obtention de positions des yeux de la personne. Le procédé comprend en outre la détection d'une ou de plusieurs fixations des yeux à partir des positions des yeux obtenues; et la mesure de l'anglie de convergence des yeux au cours du temps à partir des positions des yeux obtenues pendant une ou plusieurs fixations des yeux détectées.

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Measuring cognitive issues during orienting visual attention task

- Computerized & engaging task
- Over 100 trials; 10-12 minutes
- Cue and no-cue condition to measure attention
- We record vergence
- Classification by Machine Learning techniques

Detecting ADHD more objectively analyzing cognitive vergence using machine learning classifiers

Sole Puig et al., PloS ONE 2015 Varela et al., J Att Disorder 2018 Jimenez et al., J Att Disorder 2020 Boxhoorn et al., J Child Psych Psych 2020 Morata et al., submitted Best et al., submitted Steve Faraone et al., in prep Detecting ADHD in children more objectively analyzing cognitive vergence using machine learning classifiers

	Non-ADHD vs ADHD
Ν	159
Accuracy	92.83%
AUC	97.42
FP i.e. healthy patient diagnosed as ADHD	5.35%
FN i.e. ADHD patients classified as healthy	8.51%

ADHD classification trial in adults

Detection of MCI and Alzheimer patients

5 min oddball task

Control/MCI/Alzheimer

0.2

0.0 -0.0

0.2

0.4

ROC

0.6 False Positive Rate AUC = 0.93

1.0

0.8

Digital therapy

Interactive eye tracking serious game to train cognitive behavior

28 ADHD patients (18 boys and 10 girls)

The experimental group played game using the eye-tracker and control group played it using the mouse.

Play game for 3 weeks, 3 times per week for 30 minutes.

evidence shows that it enables reduction of symptoms

Preliminary data on recovery of vergence/pupil responses in ADHD after psychostimulants and digital treatment

Digital treatment

Improvements in ADHD patients treated with gazecontrolled games but not in patients with mousecontrolled games

Unpublished information

Psychostimulants

Improvements in medicated ADHD patients but not in unmedicated patients

Unpublished information

At home therapy uses mobile devices

Google Play

Preliminary data on Alzheimer patients treatment after 2 weeks interactive eye tracking game play

Clinical studies using our method

PARTE DE BUPO

Jimenez et al., submitted Hashemi et al., submitted

Syracuse University

Steve Faraone et al., in prep.

Vall d'Hebron

Varela et al., J Att Disorder 2018 Jimenez et al., J Att Disorder 2020 Morata et al., submitted Jimenez et al., Vis Research 2020 Sole et al., PLoS One 2015

>1300 people

involved in

13 clinical studies

Sole et al., PLoS One 2013a Sole et al., PLoS One 2013b Sole et al., Neuroreport 2016 Sole et al., PLoS One 2016 Esposito & Supèr, Neuroreport 2018 Esposito & Supèr, Acta Psychologica 2019 Sole et al., submitted

Pipeline status now

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Overlap of attention network and network of cognitive vergence

Detection of malingering ADHD in young adults

System to measure cognitive vergence

- Non-invasive and contactless
- Plug and play set-up
- Easy to administer
- Easy and short visual task
- Automatic collection of data
- Al classification of patients
- Low-cost

Attention can be measured by cognitive vergence

9

ADHD classification trial in school cohort

	Non-ADHD vs ADHD
Ν	270
Accuracy	92.0%
AUC	96
FP i.e. healthy patient diagnosed as ADHD	6.5%
FN i.e. ADHD patients classified as healthy	6.4%

Detection of reading difficulties

Children (N=215;M±SD: 9.1±1.8 years of age)

Detection of reading difficulties

40 4 Model score 3 N -0 0 2 3 5 TLK (Testing Lecture Knowledge) score

Dyslexia regressor

Psychostimulants recover vergence/pupil responses in ADHD patients towards normal levels

Supporting evidence that cognitive vergence could be used to measure effect of medication

- Wainstein G, Rojas-Líbano D, Crossley NA, Carrasco X, Aboitiz F, Ossandón T. (2017). **Pupil Size Tracks Attentional Performance In Attention-Deficit/Hyperactivity Disorder** Sci Rep. 7(1):8228. doi: 10.1038/s41598-017-08246-w.
- Fried M, Tsitsiashvili E, Bonneh YS, Sterkin A, Wygnanski-Jaffe T, Epstein T, Polat U. (2014) ADHD subjects fail to suppress eye blinks and microsaccades while anticipating visual stimuli but recover with medication Vision Res. 01:62-72. doi: 10.1016/j.visres.2014.05.004.
- Dolder PC, Müller F, Schmid Y, Borgwardt SJ, Liechti ME. (2018). Direct comparison of the acute subjective, emotional, autonomic, and endocrine effects of MDMA, methylphenidate, and modafinil in healthy subjects Psychopharmacology (Berl). 235(2):467-479. doi: 10.1007/s00213-017-4650-5.
- Grönlund MA, Aring E, Landgren M, Hellström A. (2007) Visual function and ocular features in children and adolescents with attention deficit hyperactivity disorder, with and without treatment with stimulants Eye (Lond). 21(4):494-502. doi: 10.1038/sj.eye.6702240.

Preliminary data on Control, ADHD, ASD, and ADHD+ASD

Angry

Sad

Fearful

Vergence responses

ADHD+ASD vs rest

ROC

