

# Technologies

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# Neuromodulation

# Neurofeedback

# Brain waves when we are awake

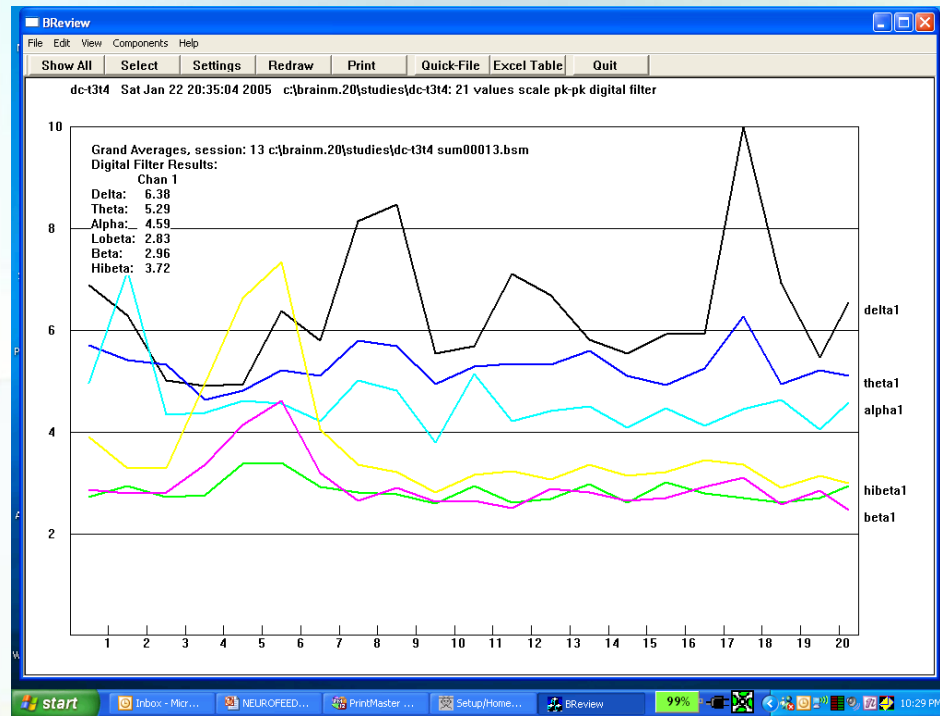
- **They are called alpha (medium), beta (fast), and theta (slow) waves:**
  - ✓ **Alpha** waves are seen when a person is in a relaxed state, and not actively thinking or interacting with one's environment.
  - ✓ **Beta** waves are present when a person is interacting with the surrounding environment, and is concentrating, thinking, or solving problems.
  - ✓ **Theta** waves are often seen during times of drowsiness, daydreaming or during light sleep, but can also occur during thoughtless, restless overactivity.
- (A fourth type of brain wave, called **delta**, is seen during deep sleep).

# QEEG

- The device **measures the ratio of power between two types of brain activity : theta and beta**
- The goal is to see which type is more powerful
- The device also measures the amount of beta power at **the front of the brain**
- This is where higher-level brain processes happen, such as thinking

# Unability to pay attention or focus

- Unusually high theta activity in the front of the brain
- Higher theta activity than beta activity



The patterns of brain wave activity varies, depending on **where on the brain** we are looking, and **what kinds of things we are doing**. In different mental states, different types of brain waves dominate.

- There are findings that many individuals with **ADHD** show **low levels of arousal in frontal brain areas**, with excess of theta waves and deficit of beta waves



# QEEG in ADHD Diagnosis

- QEEG is a method of tracking brain activity
- QEEG should not be used to diagnose ADHD
- This approach to diagnosis should only happen in the context of a research study

# QEEG in ADHD Diagnosis

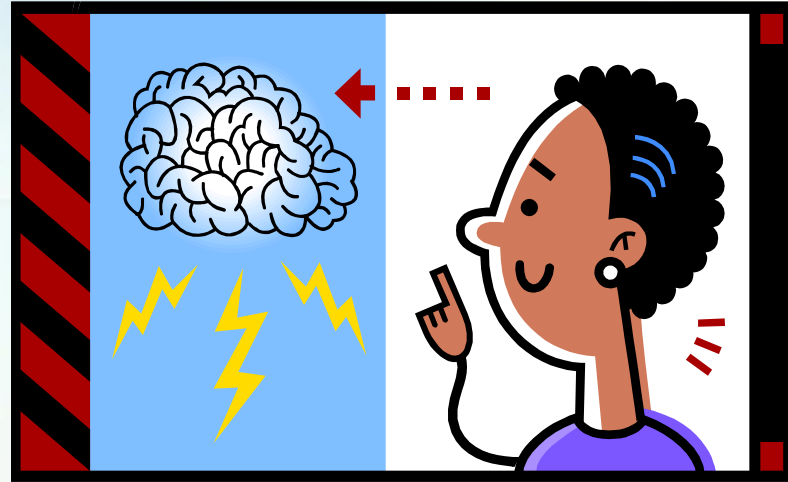
- A 2013 **meta-analysis** of nine studies (including 1253 children with ADHD and 517 without ADHD) found **significant heterogeneity** and concluded that EEG profiles (specifically an increased theta to beta ratio) **cannot be used to reliably diagnose ADHD**
- They **may be helpful for prognosis**

# Neurofeedback

- NFB is a self-paced brain neuromodulation technique
- Represents brain activity in real-time using auditory or visual modulations
- Learning paradigms, such as operant conditioning or voluntary control, can be applied.

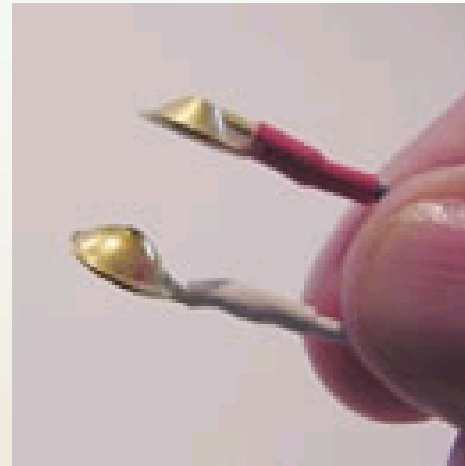
# THE BIG

# IDEA:



When you have information **what your brain waves are doing**, your brain can use that information **to change how it works.**

We can detect this electrical signal using sensors – electrodes – placed on the scalp.



This electrical signal is then magnified by some kind of amplifier, which is then fed through a computer.

BrainMaster



Wireless Pendant



Pendant with Battery, Wireless Receiver, and Electrode Adapter



Wireless receiver in USB port



Pendant as Worn



Pocket 1-W EEG

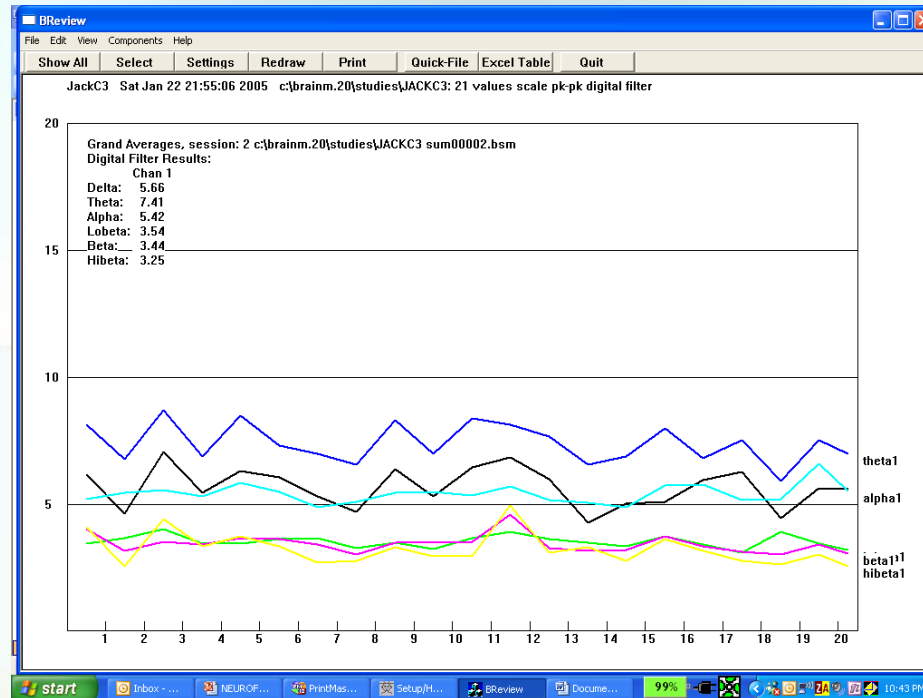
# Neurofeedback

- When the brainwaves are of the desired frequency, **the beep may inform the patient**, or the character in the game will move in the proper direction
- When **the patient has learned how to increase these arousal levels**, proponents believe improvements in attention will result and that there will be reductions in hyperactive/impulsive behavior

- The sensory feedback constitutes the **rewards mechanism**, promoting learning using, for instance, operant conditioning protocols



- Operant conditioning enables **neural plasticity**, thus supporting the child in the task repetition, which is **believed to result in long-lasting neuronal reorganization**



NF works by re-training the brain to  
**produce the beta waves on its own** –  
 and many people continue to improve  
 after the training ends!

- Several NFB protocols have been proposed and investigated for decreasing the symptoms of ADHD:
- NFB protocols can be personalized

# The recent meta-analysis addressing the efficacy of NFB

- Including a total of 13 RCTs
- Based on **parent assessments**, which are not blind to treatment, they are significantly in **favor of NFB**
- Based on **teacher assessments** (considered as probably blind), the results are **no longer significant**

# Limitations

- Lack of control groups
- Confounding variables
- Small sample sizes
- Uncertainty as to whether all the children in the studies were accurately diagnosed with ADHD
- Lack of placebo control procedures
- Absence of “blinding”
- Lack of randomization in some studies

# Canadian ADHD Practice Guideline 2018

- Under randomized placebo control conditions **no study** has shown significant effect sizes
- **Proximal raters** to the treatment condition (e.g. parents) tend to over-estimate the effect of NF when compared to more **distal, blinded raters** (e.g. teachers, research staff)
- Treatment effects are **limited yet tend to be durable over time** (when evaluated again at 6 month follow-up)

# Canadian ADHD Practice Guideline 2018

- There is insufficient data to recommend NF as a standard treatment for ADHD.

# Clinical and Experimental Factors Influencing the Efficacy of Neurofeedback in ADHD: A Meta-Analysis

- **First**, a more intensive treatment, but not treatment duration, is associated with higher efficacy
- **Second**, teachers report a lower improvement compared to parents
- **Third**, using high-quality EEG equipment improves the effectiveness of the NFB treatment



Meta-Analysis  
Eur Child Adolesc Psychiatry  
2019 Mar;28(3):293-305.

**Sustained effects of neurofeedback in ADHD: a  
systematic review and meta-analysis**

[Jessica Van Doren<sup>1</sup>](#), [Martijn Arns<sup>2 3 4</sup>](#), [Hartmut  
Heinrich<sup>1 5</sup>](#), [Madelon A Vollebregt<sup>6 7</sup>](#), [Ute Strehl<sup>8</sup>](#), [Sandra  
K Loo<sup>9</sup>](#)

- Ten studies met inclusion criteria
- Compared to non-active control treatments, NF appears to **have more durable treatment effects, for at least 6 months following treatment**

**Neurofeedback and Attention-  
Deficit/Hyperactivity-Disorder (ADHD) in  
Children: Rating the Evidence and Proposed  
Guidelines**

Martijn Arns,  
C. Richard Clark,  
Mark Trullinger,  
Roger deBeus,  
Martha Mack &  
Michelle Aniftos

*Applied Psychophysiology and  
Biofeedback* **volume 45**, pages39–48(2020)

- In this quantitative review we utilized an updated and stricter version of the APA guidelines for rating 'well-established' treatments and focused on efficacy and effectiveness **using effect-sizes (ES) and remission, with a focus on long-term effects**

- Efficacy and effectiveness are compared to medication and behaviour therapy using benchmark studies.

- **Two meta-analyses confirmed significant efficacy** of standard neurofeedback protocols for parent and teacher rated symptoms with a **medium effect size**, and sustained effects after 6–12 months
- **Four multicenter RCT's** demonstrated significant superiority to semi-active control groups, **with medium-large effect sizes** end of treatment or follow-up and remission rates of 32–47%

# Standard neurofeedback protocols in the treatment of ADHD

- a well-established treatment
- medium to large effect sizes
- 32–47% remission rates
- sustained effects as assessed after 6–12 months

# The first FDA-approved device to treat ADHD

- **Monarch eTNS system**

(external trigeminal nerve stimulation)

- One 5-week randomized controlled trial with just 30 participants receiving eTNS



Randomized Controlled Trial  
J Am Acad Child Adolesc Psychiatry 2019

**Double-Blind, Sham-Controlled, Pilot Study of  
Trigeminal Nerve Stimulation for Attention-  
Deficit/Hyperactivity Disorder**

James J McGough<sup>1</sup>, Alexandra Sturm<sup>2</sup>, Jennifer  
Cowen<sup>2</sup>, Kelly Tung<sup>2</sup>, Giulia C Salgari<sup>2</sup>, Andrew  
F Leuchter<sup>2</sup>, Ian A Cook<sup>3</sup>, Catherine A  
Sugar<sup>4</sup>, Sandra K Loo<sup>2</sup>

- Trigeminal nerve stimulation (TNS), a minimal-risk noninvasive neuromodulation method



# Method

- **Sixty-two children 8 to 12 years** old, with full-scale IQ of at least 85 and Schedule for Affective Disorders and Schizophrenia-diagnosed ADHD, were **randomized to 4 weeks of nightly treatment with active or sham TNS**, followed by 1 week without intervention
- Assessments included weekly clinician-administered **ADHD Rating Scales (ADHD-RS)** and Clinical Global Impression (**CGI scales**) and quantitative electroencephalography at baseline and week 4.

- This study demonstrates TNS efficacy for ADHD in a blinded sham-controlled trial, with estimated treatment **effect size similar to non-stimulants**
- TNS is well tolerated and has minimal risk.

# The most common side effects

- ✓ drowsiness
- ✓ an increase in appetite
- ✓ trouble sleeping
- ✓ teeth clenching
- ✓ headache and fatigue
- ✓ No serious adverse events were associated with use of the device

# Contraindications of eTNS

- children under seven years of age
- patients with an active implantable pacemaker or with active implantable neurostimulators
- Patients with body-worn devices such as insulin pumps
- in the presence of radio frequency energy such as magnetic resonance imaging (MRI)

# tDCS

- A **non-invasive**, painless brain stimulation treatment that uses direct electrical currents to stimulate specific parts of the brain
- A constant, **low intensity current** is passed through two electrodes placed over the head which modulates neuronal activity
- There are two types of stimulation with tDCS: **anodal and cathodal stimulation**
- Anodal stimulation acts to excite neuronal activity while cathodal stimulation inhibits or reduces neuronal activity

# Difference between ECT and tDCS

- جریان الکتریسیته ضعیف تر
- مدت زمان طولانی تر (20-30 دقیقه)
- عدم ایجاد تشنج به دلیل زمان طولانی تر برای سازگاری مغز



# Transcranial Direct Current Stimulation in ADHD: A Systematic Review of Efficacy, Safety, and Protocol-induced Electrical Field Modeling Results

Mohammad Ali Salehinejad,

Vahid Nejati,

Mohsen Mosayebi-Samani,

Ali Mohammadi,

Miles Wischnewski,

Min-Fang Kuo,

Alessio Avenanti,

Carmelo M. Vicario &

Michael A. Nitsche

*Neuroscience Bulletin* **volume 36**, pages 1191–  
1212(2020)

# tDCS in ADHD

- a literature search identified **14 empirical experiments** investigating tDCS effects in ADHD
- **Partial improving** effects of tDCS on cognitive deficits (response inhibition, working memory, attention, and cognitive flexibility) or clinical symptoms (e.g., impulsivity and inattention) are reported **in 10 studies**
- No serious adverse effects are reported in 747 sessions of tDCS.

- **The clinical utility of tDCS in ADHD cannot yet be concluded** and requires further systematic investigation in larger sample sizes

# An FDA-Approved Game

- [EndeavorRx](#), is a game-based digital therapeutic device from Akili Interactive to help improve attention

- The device is intended for children **ages 8-12** years old and requires a prescription
- It is intended to be **used along with other treatment** modalities including therapy, medication and/or education programs

- The device was tested in more than 600 children across several studies including a randomized controlled trial detailed in [\*The Lancet Digital Health\*](#)
- That study found improved attention with no serious adverse events
- The most common adverse events were **frustration, headache, dizziness, emotional reaction and aggression**

Thank You! – Any Questions?

