### Cognitive interventions in youth with ADHD

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- Attention deficit hyperactivity disorder (ADHD) is the most common neurodevelopmental disorder in children
- Although not considered a diagnostic criterion in DSM-V, cognitive difficulties in children with ADHD are commonly reported.

### Neural circuits in ADHD

- fronto-striatal circuit : executive cognitive functions, and its dysregulation causes deficits in sustained attention, organization, planning, working memory, and motor response inhibition
- fronto-limbic circuits : is associated with symptoms of hyperactivityimpulsivity, delay aversion, aggression, motivation, and emotional dysregulation
- fronto-cerebellar circuits : motor coordination deficits and problems with the timing and timeliness of behavior

- Clinical relevance of cognition enhancing effects of interventions is limited.
- Interventions that improve ADHD symptoms have mixed effects on cognitive deficits.
- individual differences are a serious concern
- the cause of cognitive and behavioral deficits in children with ADHD is quite varied
- Refining ADHD endophenotypes may improve links between cognition and treatment

### **Cognitive training**

- aged 7 to 12
- 20 days of training
- computer program for training working memory(WM )or a comparison program
- This study shows that WM can be improved by training in children with ADHD. This training also improved response inhibition and reasoning and resulted in a reduction of the parent-rated inattentive symptoms of ADHD.

### **Cognitive training**

Met analysis:

- in the preschool period :
- improvement of executive function( EF) performance
- reducing ADHD and ODD symptoms

# Repetitive transcranial magnetic stimulation (rTMS)

- Limitations : Heterogeneity in stimulation parameters, patient age and outcome measures limited the interpretation of findings.
- (rTMS) can produce effects on dopaminergic system similar to effects of amphetamine
- TMS-evoked EEG potentials (TEPs) could present a well-suited marker for realtime monitoring. Monitoring is particularly important in children where only few data about rTMS effects and safety are currently available.

### specific contraindications of rTMS

- any metallic object implanted in the skull (with the exception of oral dental devices)
- an implanted medication pump or cochlear implant
- implanted intra-cardiac lines or pacemaker
- factors that might increase the risk of seizure with TMS such as a history of a seizure disorder, febrile seizures during childhood, known brain lesions, or a history of major head trauma involving loss of consciousness for more than 5 min
- alcohol use during the previous night of TMS treatment, was associated with seizure induction

- right dorsolateral prefrontal cortex (DLPFC) hypoactivity in ADHD during inhibitory control and attentional tasks
- increasing the excitability of the right DLPFC through high-frequency rTMS can improve ADHD symptoms

- 7-12years ADHD
- nonresponsders to conventional therapy
- 1 Hz rTMS
- Iow-frequency rTMS applied to the L-DLPFC and high-frequency rTMS applied to the R-DLPFC
- may target inattention, hyperactivity, and impulsivity.

- 60 children with ADHD
- 30 participants : 15 sessions of rTMS over the R-DLPFC combined with Atomoxetine 1.2 mg/kg/day
- 30 participants: 15 sessions of sham rTMS and atomoxetine 1.2 mg/kg/day
- Clinical assessments of ADHD symptoms and severity were done and compared at 3 points, before treatment, after and follow-up 1 month
- ▶ 5 sessions per week, for 15 sessions
- rTMS is an efficacious intervention for treating ADHD, and combined rTMS and atomoxetine is superior to atomoxetine alone in improving attention deficit symptoms and total ADHD symptoms severity.

- 60 children with ADHD
- 30 daily 25-min sessions of 10Hz rTMS over R-DLPFC, Atomoxetine (1.2mg/kg), or combined treatment over 6 weeks
- rTMS, ATX, or rTMS combined with ATX can effectively alleviate attention deficit, hyperactivity impulse, and oppositional defiance in ADHD children
- the combined treatment is more effective than using Atomoxetine

- 6 to 12 years old
- All patients on the sample were not receiving any medical or behavioral therapy for ADHD
- means scores of inattention, hyperactivity and impulsivity were reduced significantly in the post 5 days and 2 weeks follow up
- started to rise again in its evaluation after 4 weeks but not reaching its values before rTMS sessions
- no patient experienced any significant adverse effects during the study, except 3 children reported mild headache that resolved spontaneously within an hour without medication

## transcranial direct current stimulation (tDCS)

- Individuals with ADHD have deficits in reward processing and related cognitive tasks such as delay discounting and risky decision-making
- The ventromedial prefrontal cortex (vmPFC) and dorsolateral prefrontal cortex (dlPFC) are two distinct cortical areas that are involved in reward processing
- Right prefrontal hypo activation successfully distinguished ADHD patients from healthy controls
- right IFG is the brain area that shows the most consistent activation increase after the application of methylphenidate



- tDCS alters neuronal resting membrane potentials, and depending on the stimulation polarity, enhances or reduces excitability of the cortical activity.
- The excitability and plasticity alterations as a result of tDCS allow alteration of various brain processes and cognitive functions (i.e., learning, attention, memory)

Partial improving effects of tDCS on:

 cognitive deficits (response inhibition, working memory, attention, and cognitive flexibility)

or clinical symptoms (e.g., impulsivity and inattention)

- The left and right dorsolateral prefrontal cortex are the regions most often targeted
- electrical field induced by 1 mA, which is likely larger than the electrical field induced by 1 mA in adults due to the smaller head size of children

- anodal HD-tDCS that was repetitively applied to the right IFG over five consecutive days in 10-17 Y with ADHD 4-month follow up:
- higher improvements of working memory, response inhibition and attention
- about half of the patients reported painful sensations when receiving tDCS at a current intensity of 0.5 mA

- ADHD children
- 10 sessions
- The current intensity was 1 mA for 15 min with a 72-hr interval between sessions:
- Anodal left DLPFC tDCS most clearly affected executive control functions (e.g., WM, interference inhibition), while cathodal left DLPFC tDCS improved inhibitory control :
- Task-specific stimulation protocols can improve EFs in ADHD.



- In children with ADHD, anodal tDCS over the right DL-PFC induces more conservative and less impulsive decisions
- anodal tDCS over the L-DLPFC enhanced efficacy of working memory performance

- Impaired executive functions in ADHD are associated with hypoactivity of the right inferior frontal gyrus(IFG)
- anodal, high-definition tDCS
- five consecutive days
- 0.5 mA or 0.25 mA depending on individual cutaneous sensitivity
- During stimulation, participants performed a combined working memory and response inhibition paradigm
- distinct effects of tDCS with different current intensities demonstrating the importance of a deeper understanding on the impact of stimulation parameters and repeated tDCS applications to develop effective tDCS-based therapy approaches in ADHD.

two studies investigated repeated applications of tDCS in ADHD for five consecutive days demonstrating promising effects on ADHD symptom severity, which were still present 1-4 weeks after the intervention

- multi-session anodal-tDCS over R-IFC combined with (Cognitive Training) CT in double-blind, randomized ,sham -controlled trial Fifty boys with ADHD (10-18 years) received 15 weekday sessions of
- anodal or sham- tDCS over R-IFC combined with CT (20 min, 1 mA):
- no evidence of improved ADHD symptoms or cognitive performance

When prefrontal brain activity is enhanced using anodal tDCS this may improve executive functioning in children and adolescents with ADHD

- repeated tDCS applications of six or seven sessions can induce effects that last up to 6 or 12 months
- As tDCS was demonstrated to interact with endogenous plasticity mechanisms it seems to be most effective when applied simultaneously with a cognitive task



- Electrophysiological assessments via electroencephalography (EEG) allow the investigation of tDCS induced alterations in neural processes beyond behavioral measures
- > P3 amplitude reductions belong to the most sensitive biomarkers for ADHD

with only few and mild side effects, which are mostly tingling and itching skin sensations

### Neurofeedback (NF)

- We identified 21 studies: Two-thirds involved θ/B EEG marker modulation, and one-third modulation of slow cortical potentials.
- NF significantly improved ADHD symptoms but did not systematically improve disruptive behaviors
- NF may work by fixing the underlying cognitive problems in ADHD instead of just improving symptoms
- Patients with more difficulty efficiently integrating information and paying auditory attention seem especially likely to improve with NF

- NF has been shown to have positive and long-lasting effects on ADHD symptoms, significantly improving behavior, attention, reaction times, with related benefits in motor control and bimanual coordination, which are often problematic in children with ADHD
- children with ADHD have a higher theta/alpha ratio, in addition to the theta/beta ratio
- individual variability in the EEG can influence irrelevant areas of the brain if not taken into account

- NF protocols may need to emphasize sound-based tasks more to optimize gains
- the results support NF as an alternative or extra therapy to stimulant meds.
- Showing NF impacts brain function like medication does is promising for NF as a non-drug option targeting underlying ADHD issues
- QEEG-informed selection of NF protocol improves the efficacy of NF

- **TBR, SCPs, and SMR NF protocols are most commonly used for treating ADHD**
- TBR NF (reducing the theta/beta ratio) is not indicated for ADHD with comorbid anxiety but may benefit ADHD with ODD
- reducing the theta/beta ratio represents the main choice for the treatment of ADHD

- personalized NF is more effective in improving attention and impulse control in children with ADHD than the standard protocol
- 30 weekly sessions : NF combined with computer cognitive games (CCGs) can improve time perception, attention, and working memory in children with ADHD
- the effect is more long-lasting when combined with simultaneous EMG control

### electromyographic BF (EMG-BF)

- EMG signal generated by the forehead muscles could explain the poor efficacy of NF in ADHD.
- Elevated forehead muscle tone is considered a sign of psycho emotional tension or mental stress, which may be present in ADHD, and this has led to the hypothesis that :
- the effectiveness of NF treatment may further increase if combined with a practice of EMG-BF

#### EMG-BF

- 30 treatment sessions:
- NF to reduce the theta/beta ratio and EMG-BF aimed at relaxing the frontal muscles :
- NF group effectively reduced theta/beta ratios and EMG level
- BF achieved a positive impact similar to NF

#### EMG-BF

HRV training showed that :

this treatment helps reduce several behavioral symptoms of ADHD

### THE END