Effects of TMS on Autonomic Nervous System in Children with Autism

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Introduction & Background

- Autism is a pervasive developmental disorder (prevalence is 1 in 150) marked by difficulty in social interaction, impairments or lack of communication, and restricted range of interests. Many children with autism exhibit symptoms associated with autonomic dysfunction, which is abnormalities in regulation of blood pressure, temperature, heart rate, and all other body functions by the autonomic nervous system (ANS).
- The main findings of autonomic abnormalities studies in Autism Spectrum Disorders (ASD) point at reduced baseline parasympathetic activity in children with autism, while parasympathetic activity remains stronger in HF.
- Sympathetic influences are reflected in VLF and LF components of HRV, while inhibitory parasympathetic ANS inputs: rTMS with autism and in typically developing children. Another aim of the study was to investigate differences in physiological measures reflecting autonomic nervous system (ANS) activity in children with autism and in typically developing children.
- Hypotheses to be tested in the study were (1) low frequency (0.5 Hz) rTMS of frontal cortex may lower ANS hyper-activation in children with autism through activation of frontal inhibitory tone controlling ANS, and (2) lower ANS after post-TMS will be manifested in decrease of skin conductance level (SCL), heart rate (HR), and increased HR variability.

Methods: repetitive TMS

- Administration of repetitive TMS in children with autism
  - During each session, patients were seated in a comfortable chair and wore a swap cap and ear plugs while a trained electrophysiologist delivered TMS using a Magstim Model 220 instrument (Magstim Corp., England) using a 70-mm wing span figure-eight coil. Motor threshold (MT) was determined by administering mild supra-threshold stimulations administered over the left motor cortex to determine the optimal area for stimulation of the adductor pollicis brevis (APB) muscle. The output of the machine was decreased by 2% each time until the least amount of machine power that induces a 50 μV deflection, or a visible twitch, is identified in 5 out of 10 trials over the cortical area controlling the contralateral APB. Surface electrodes were attached over the forehead (dorsal forehead area) as reference electrodes.
- Post-TMS measures showed a decrease of LF component of HRV (linear regression r²=0.54, P=0.042) and increased LF component of HRV (linear regression r²=0.52, P<0.046), and linear regression of SCL across sessions (F=5.48, P=0.032). This suggests a reduced sympathetic tone after TMS course resulting in a lower HR predominantly through withdrawal of sympathetic tone. However, effects of rTMS on parasympathetic tone cannot be excluded either as during 8 min of rTMS sessions HF of HRV showed statistical increase.

Results: Baseline Autonomic Group Differences (Autism vs. Controls): Pilot Study

- During 12 session long rTMS course regression analysis show significant decrease of Heart Rate and LF component of Heart Rate Variability in children with autism.
- According to the Receptive Behavioral Scale (RBS) (Ruth et al., 1999), there was a significant reduction in repetitive behavior as a result of bilateral rTMS treatment (F=2.73, P=0.014).

Results: Automatic measures Post-TMS

- Post-TMS behavioral differences post 12 rTMS sessions
  - Autonomic changes post 12 rTMS sessions showed a decrease of LF component of HRV (linear regression r²=0.54, P=0.032) with statistical changes in HR regression (F=4.52, P=0.036), without any significant changes in HF of HRV, SCL, or SKT.
- Analysis of autonomic measures showed sytematic reductions in children with ASD compared to healthy controls. rTMS course in the same children with autism. Post-12 rTMS measurements showed a decrease of LF component of HRV (linear regression r²=0.54, P=0.032) with statistical changes in HR regression (F=4.52, P=0.036), without any significant changes in HF of HRV, SCL, or SKT.

Subjects

- In this study, we investigated the activity of the autonomic nervous system in 19 children with ASD (mean age 13.9 years, SD=1.8) and 21 control subjects (16.8 years, SD=5.2). Participants with ASD were recruited through the University of Louisville Wynniosk Child Evaluation Center (WCCE). Diagnosis was made according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) and further ascertained with the Autism Diagnostic Interview-Revised (ADI-R) (Lord et al. 2003) by Dr. Sears, who also did pre- and post-TMS clinical evaluations.
- All participants were high-functioning children with ASD and full-scale IQ > 80 assessed using the Wechsler Intelligence Scale for Children, Fourth Edition (WISC-IV; Wechsler 2003).
- Participating subjects and their parents (or legal guardians) were provided with all information regarding the study, and the consent and assent forms approved by the IRB were reviewed and signed.
- Sixteen ASD subjects out of 19 participated in 18 session rTMS trial.
- Control children were recruited by ads and did only ANS assessment.

Post-TMS Behavioral Clinical Evaluations

- Autonomic Activity Changes post 18 rTMS sessions
  - During 18 session long rTMS course regression analysis show significant decrease of Heart Rate and LF component of Heart Rate Variability in children with autism.
  - According to the Receptive Behavioral Scale (RBS) (Ruth et al., 1999), there was a significant reduction in repetitive behavior as a result of bilateral rTMS treatment (F=2.73, P=0.014).

Results: Heart Rate and Heart Rate Variability components changes following TMS

- There was a significant reduction in heart rate variability as a result of bilateral rTMS (F=5.69, P=0.012).

Summary of Results

- We investigated autonomic nervous system activity in 19 children with Autism (ASD) and 21 typically developing subjects. Physiological activity measures such as skin conductance level (SCL), heart rate (HR), HRV, and skin temperature (SKT) were recorded during resting state with a C-2 J&J Engineering Inc. and Nexus-10 Medial Media B. V. monitors.
- Analysis of autonomic measures showed systematic reductions in children with ASD compared to healthy controls. E.g., autonomic measures showed significant reductions in children with ASD compared to healthy controls. E.g., lower baseline LF component of HRV, higher SCL (7.3 ± m) in controls (F=5.48, P<0.01), and a lower LF component of HRV (linear regression r²=0.54, P=0.032) with statistical changes in HR regression (F=4.52, P=0.036), without any significant changes in HF of HRV, SCL, or SKT.

Methods: ANS Activity Measurements

- Acquisation of physiological data
  - Physiological activity measures such as EMG, skin conductance level (SCL), heart rate (HR), Heart Rate variability (HRV), and skin temperature (SKT) were recorded during resting state with a C-2 J&J Engineering Inc. (WA) psychophysiological monitor. Sampling rate in both devices was set at 1024 Hz. Analysis of HRV was conducted using Kubios (Helsinki, Finland) software.

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