

Noninvasive EEG-EKG guided trans-magnetic stimulation at natural resonance frequency in children with autism: randomized double-blinded pilot study

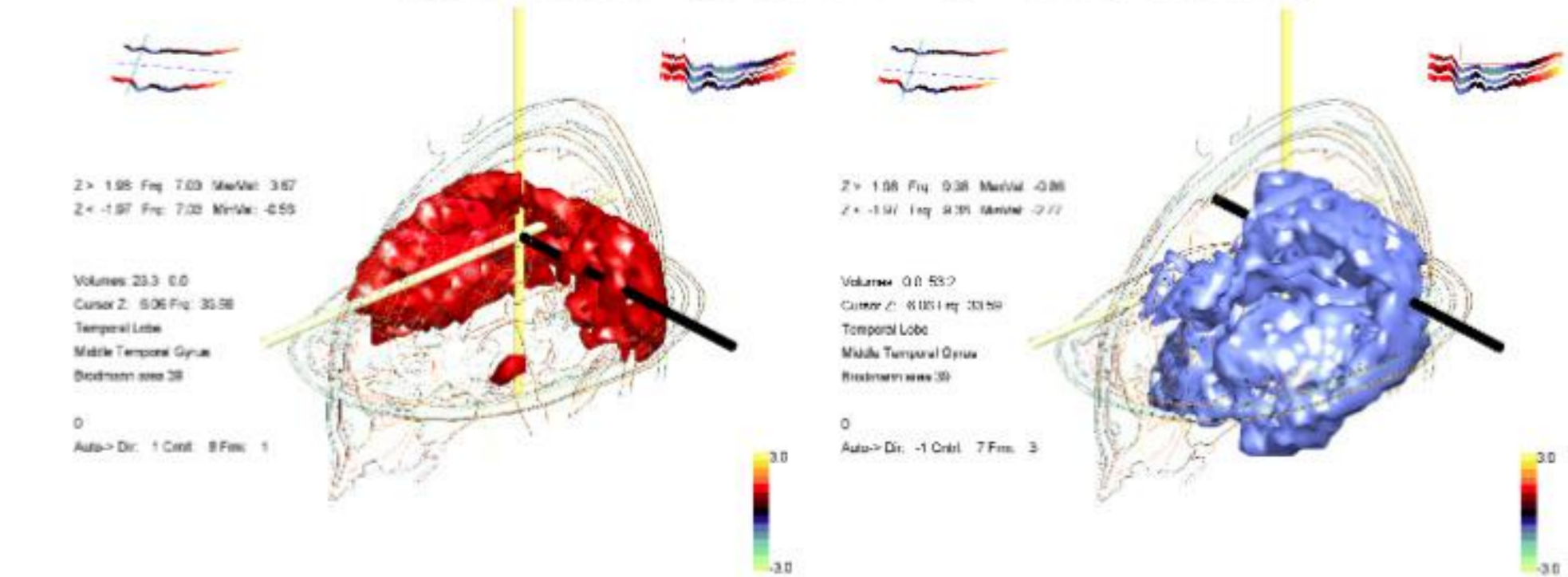
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Introduction

EEG abnormalities of the neocortex exist in autism spectrum disorder (ASD) when compared with neurotypic EEGs of the same age group (public database ¹). Particularly, cortical-to-cortical coherences inherent in normal children may be disrupted in ASD ². Transmagnetic stimulation (TMS) is a non-invasive modality that may be able to alter baseline EEG patterns, thereby improving cortical connectivity ³. We hypothesize clinical improvement in patients with ASD coinciding with changes in EEG measures.

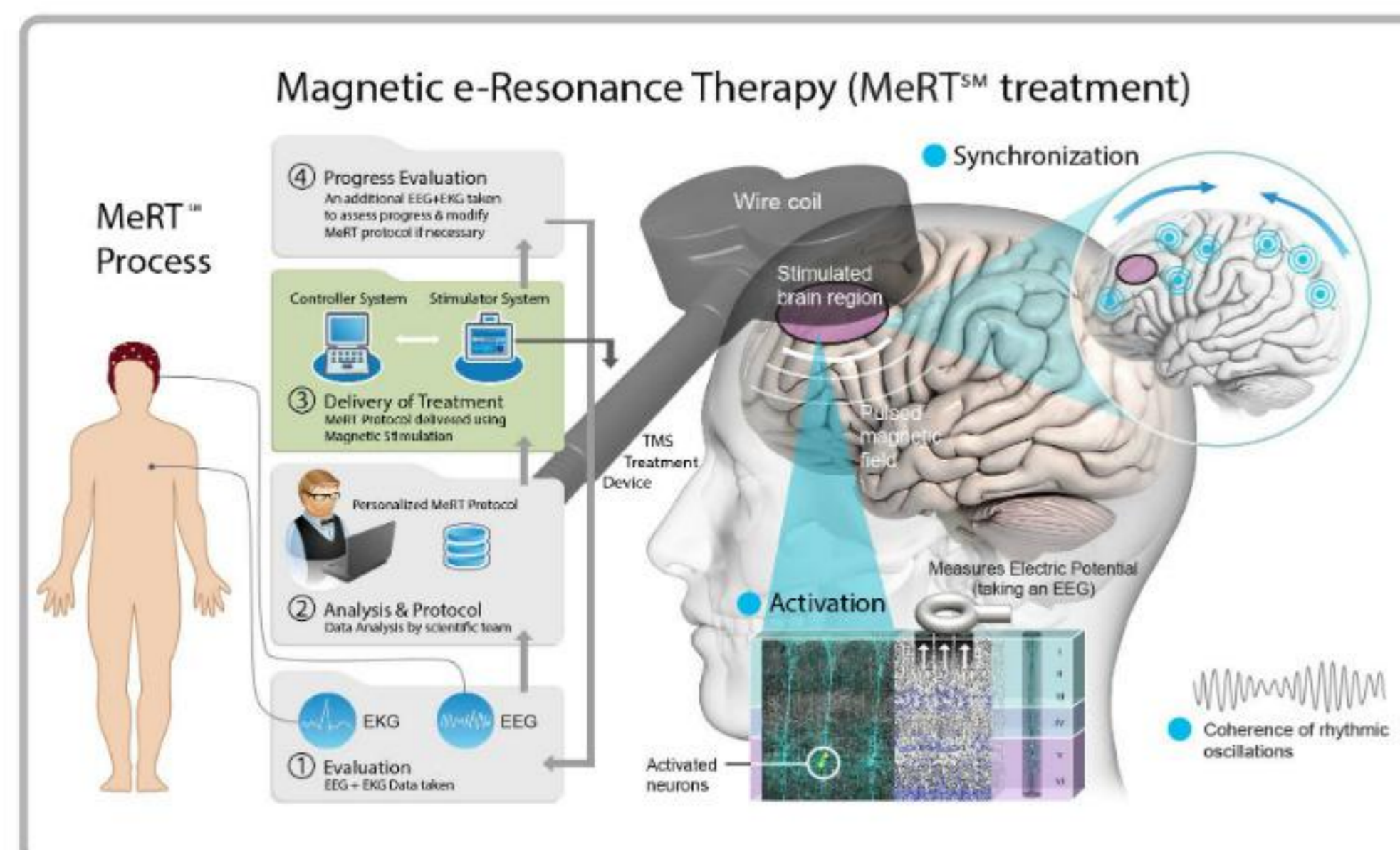
Low resolution brain electromagnetic tomography (LORETA) of dominant EEG frequencies compared with normative database



LORETA of 11-year old patient with autism demonstrating abnormally high theta distribution throughout the right posterior temporal and bilateral occipital regions (excess is marked in red; Z score ≥ 1.95). LORETA of same patient as (a) now demonstrating deficit of alpha power in the left temporal and (b) occipital regions compared to norm (deficit is marked in blue; Z score < -1.95)

Methods

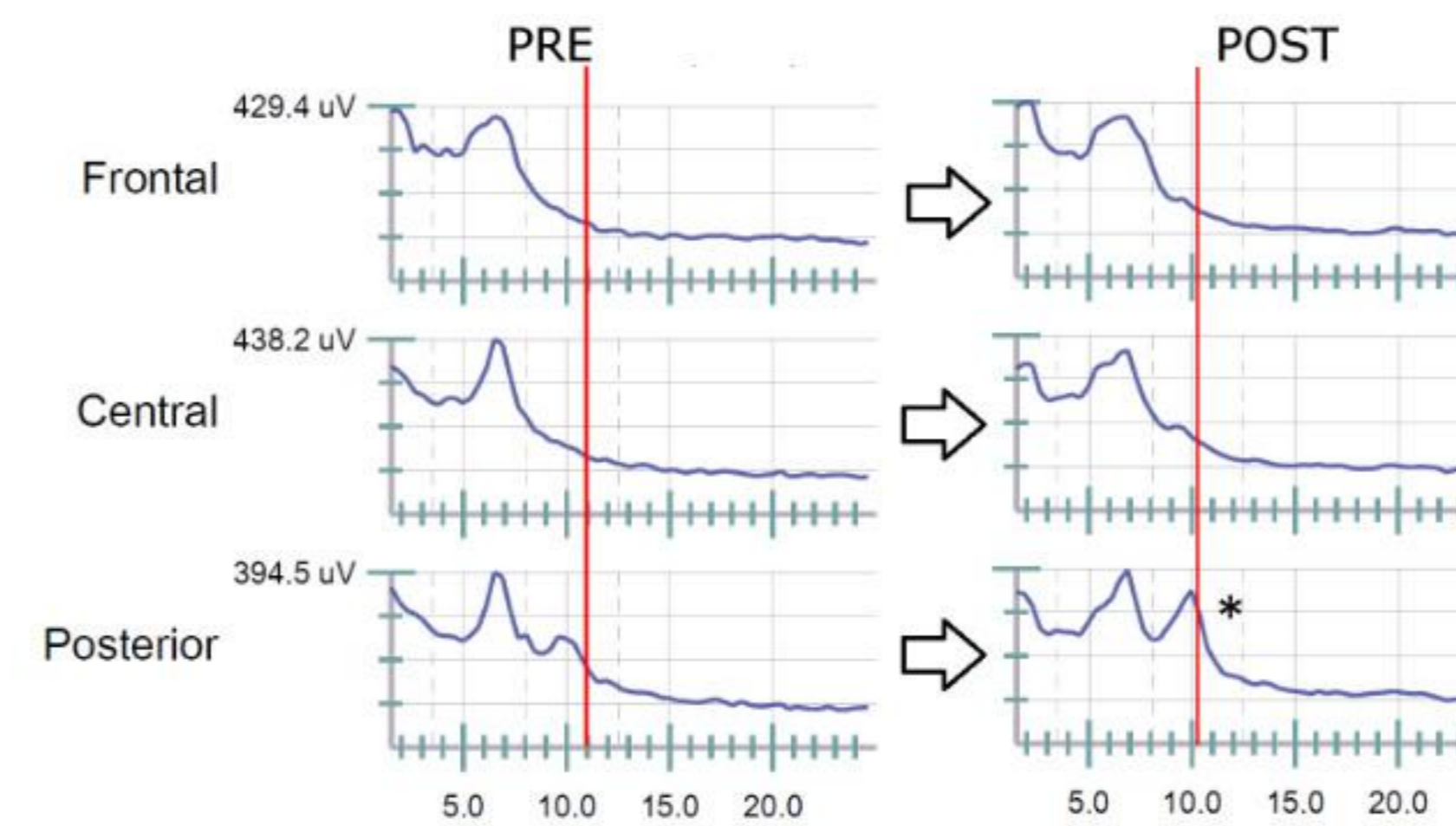
28 children with moderate to severe ASD were included in a randomized, double-blinded, placebo-controlled clinical trial. In Phase 1, children were divided randomly into treatment versus sham group and treated with EEG-EKG guided transmagnetic stimulation (MeRT) daily for 5 weeks. In Phase 2, all children were treated openly for an additional 5 weeks. Subjects' EEG, QEEG, FFT and symptoms were scored at baseline and every 2 weeks and compared with existing normative data ¹ for same age group. EEG and EKG were used to determine the treatment frequency for TMS, typically the computed dominant natural resonant frequency, f_{NR} , for each child. One-year clinical follow-up was obtained. EEG variables frequency band variables were calculated (scalp electrode grid 19x19 matrix) for each child for each EEG obtained ^{4 5}. P-values were obtained comparing EEG measures over time with treatment versus sham.



Results

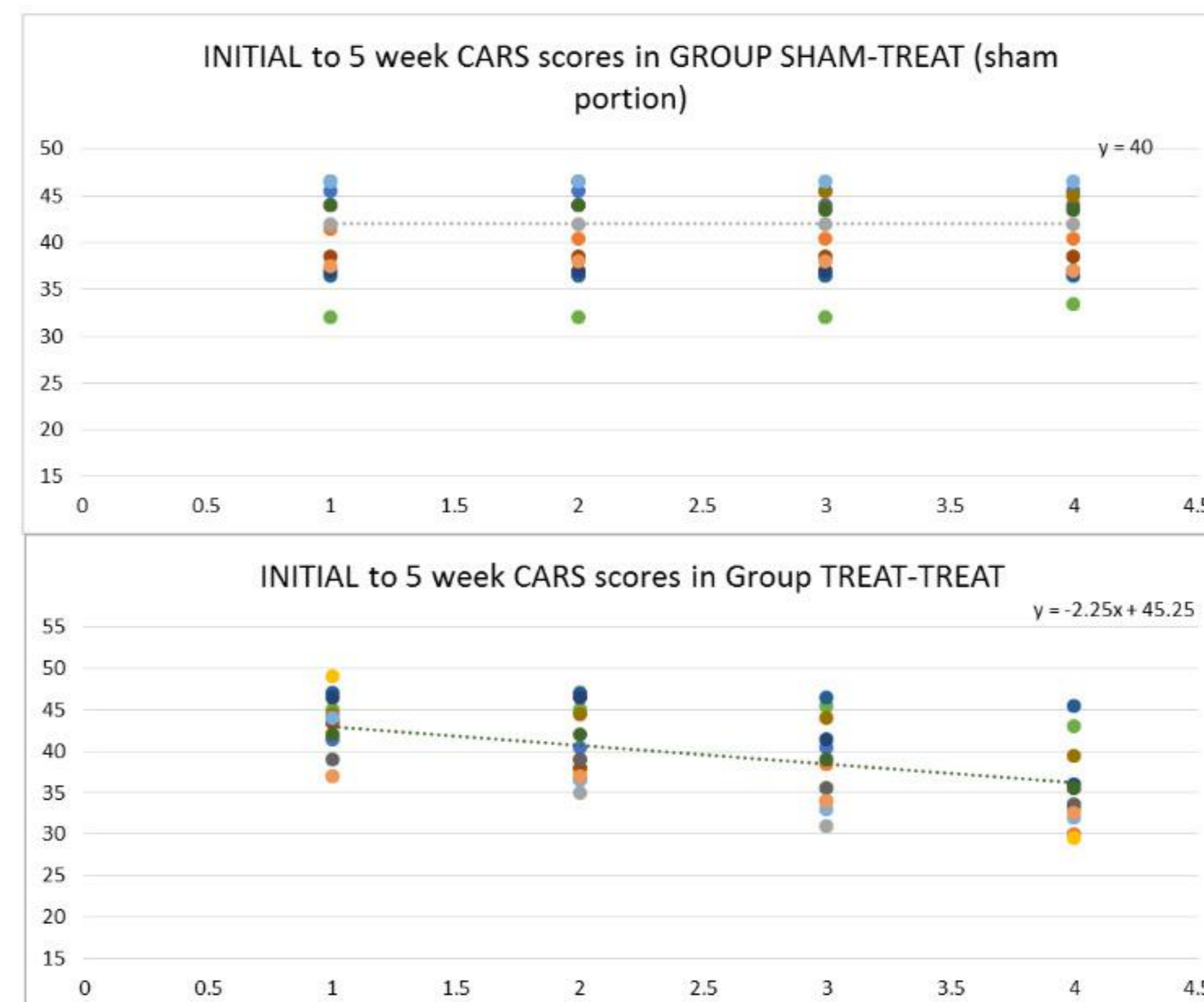
10 of 14 patients who received 5 weeks of MeRT showed >5 points CARS2-ST reduction versus 0 of 14 patients who received 5 weeks of sham ($p < 0.01$). After open label, 23 of 28 children showed CARS score reduction > 5 points (82%). In particular, improvements were noted in sensory perception as supported by CARS2-ST. Cortical coherence and phase lag coherences were significantly altered across bands following treatment ($p \leq 0.05$) when compared to sham. EEG measures showed a shift towards normotypical.

Changes in resting EEG



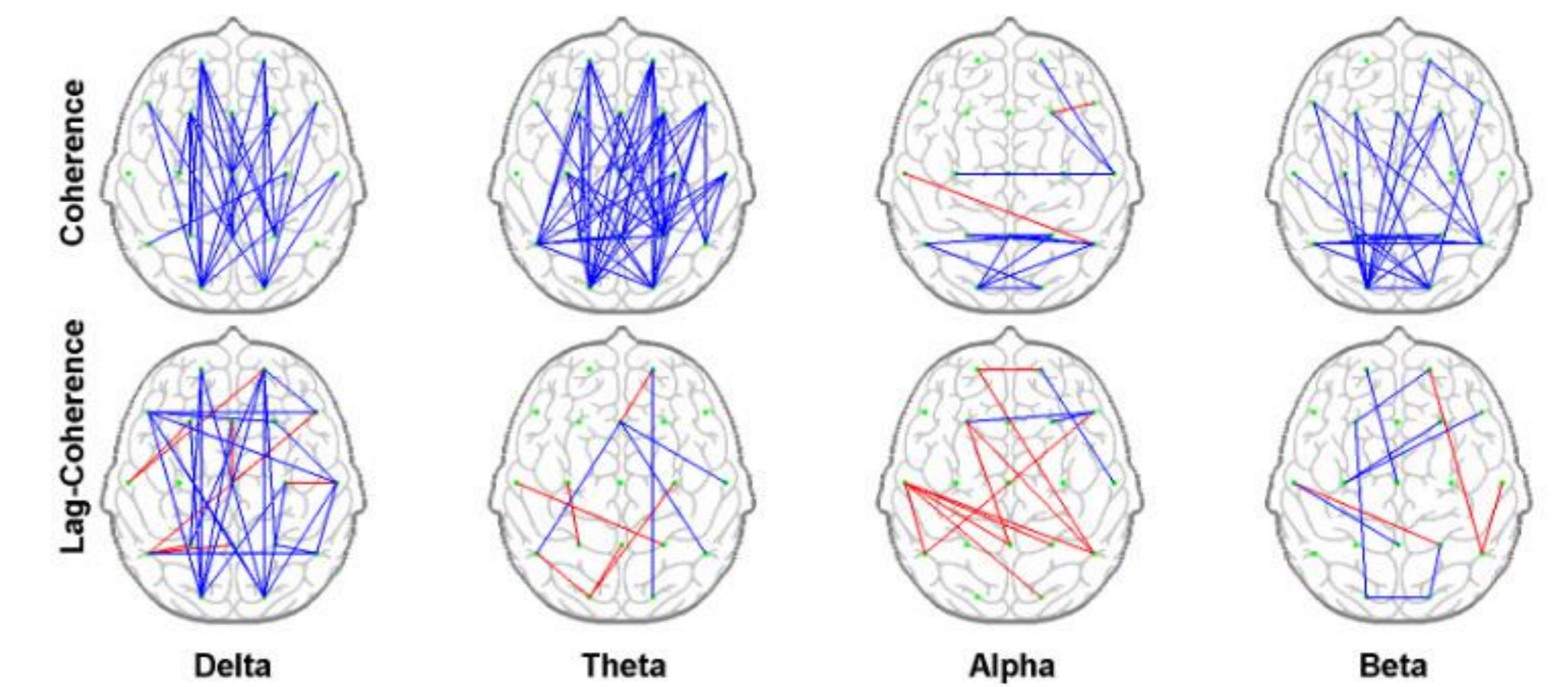
Fast fourier transform (FFT) of clean eyes-closed EEG data at baseline (Pre) and following (Post) 2 weeks, 10 sessions, of EEG/EKG-guided transmagnetic stimulation. Frontal, central and posterior EEG leads were averaged to generate regional FFTs. The red line indicates f_{NR} , the frequency calculated for therapy. Note the development of a prominent activity in the posterior region near the treated frequency following 10 sessions (*).

CARS2-ST Changes over 5 Weeks



Linear regression analysis of CARS2 scores over 5 weeks of therapy. Clinical symptom scores were significantly reduced in treated group versus sham ($p < 0.05$).

Coherence Measures Post-5 Weeks MeRT Therapy Sham+Treat



Wire-mesh headmaps describing all inter-electrode coherence and phase-lag coherence measurements. Blue lines indicate a significant reduction, whereas red lines indicate an increase ($p < 0.05$). Group TREAT-TREAT and SHAM-TREAT EEGs were combined for the data points prior to, and following 5 weeks of MeRT therapy ($n=21$). Note general reduction in coherence measures in delta and theta bands, with an increase in coherence in phase lag coherence in the alpha band.

Discussion

Following 5 weeks of EEG-EKG guided transmagnetic stimulation, significant changes in symptom severity and EEG measures are reported for 28 children with autism spectrum disorder. Parents reported most improvements in CARS2 subdomains II "imitation," III "emotional response," IV "body use," VI "adaptation to change" and IX "taste, smell, and touch responses and use". This suggests that EKG-EEG-guided TMS may be effective at mitigating aversive sensory misperceptions common in ASD. Majority of children who improved were of ages slightly less than 7, rather than pre-adolescents. Improvements were noted in a 'short' 10 week window and counter to natural ASD developmental trajectories ⁶. There was also no significant correlation between initial CARS score and amount of CARS reduction. We were able to achieve EEG changes while maintaining output intensity at less than or equal to 80% of motor threshold. Given the low n, however, further studies will be necessary.

References

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