

EVALUATION OF THETA BURST TRANSCRANIAL MAGNETIC STIMULATION AS AN ADJUNCT TO STANDARD THERAPY IN IMPROVING CORE FUNCTION DEFICITS IN CHILDREN 5-15 YEAR AGE WITH AUTISM SPECTRUM DISORDER- A RANDOMISED, DOUBLE BLIND, SHAM CONTROLLED TRIAL



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Introduction

- Autism spectrum disorder (ASD) - neurodevelopmental disorder - varying degrees of severity characterized by core deficits in social communication and interaction; and repetitive behaviour with restricted interests and activities.
- Lifelong disorder with onset in early developmental period, with effects persisting into adulthood.
- Current management strategies are time taking and labor intensive or are limited by adverse effects and proof of efficacy has not been established for many alternative therapies.

Aims and objectives

- To evaluate the efficacy of Theta Burst Transcranial Magnetic Stimulation (TBS) as an adjunct to standard therapy in children with ages 5 – 15 years with Autism Spectrum Disorder, in comparison to standard therapy alone in reducing the severity of core function deficit, at **4 weeks* from end of therapy**
- Difference of mean total RBS-R (Repetitive Behavior scale Revised) and CY-BOCS (Children's Yale-Brown Obsessive Compulsive Scores)** between intervention and Sham group at 4 weeks* from end of therapy
- Other measures used were **SRS2(Social Responsiveness Scale-2), CARS-2 (Childhood Autism Rating Scale-2), PedsQL (Pediatric Quality of life)**. Executive and cognitive skills assessed by time to Stroop and Wisconsin Card Sorting test. qEEG pre and post therapy was evaluated in a subset (n=10)

Material & Methods

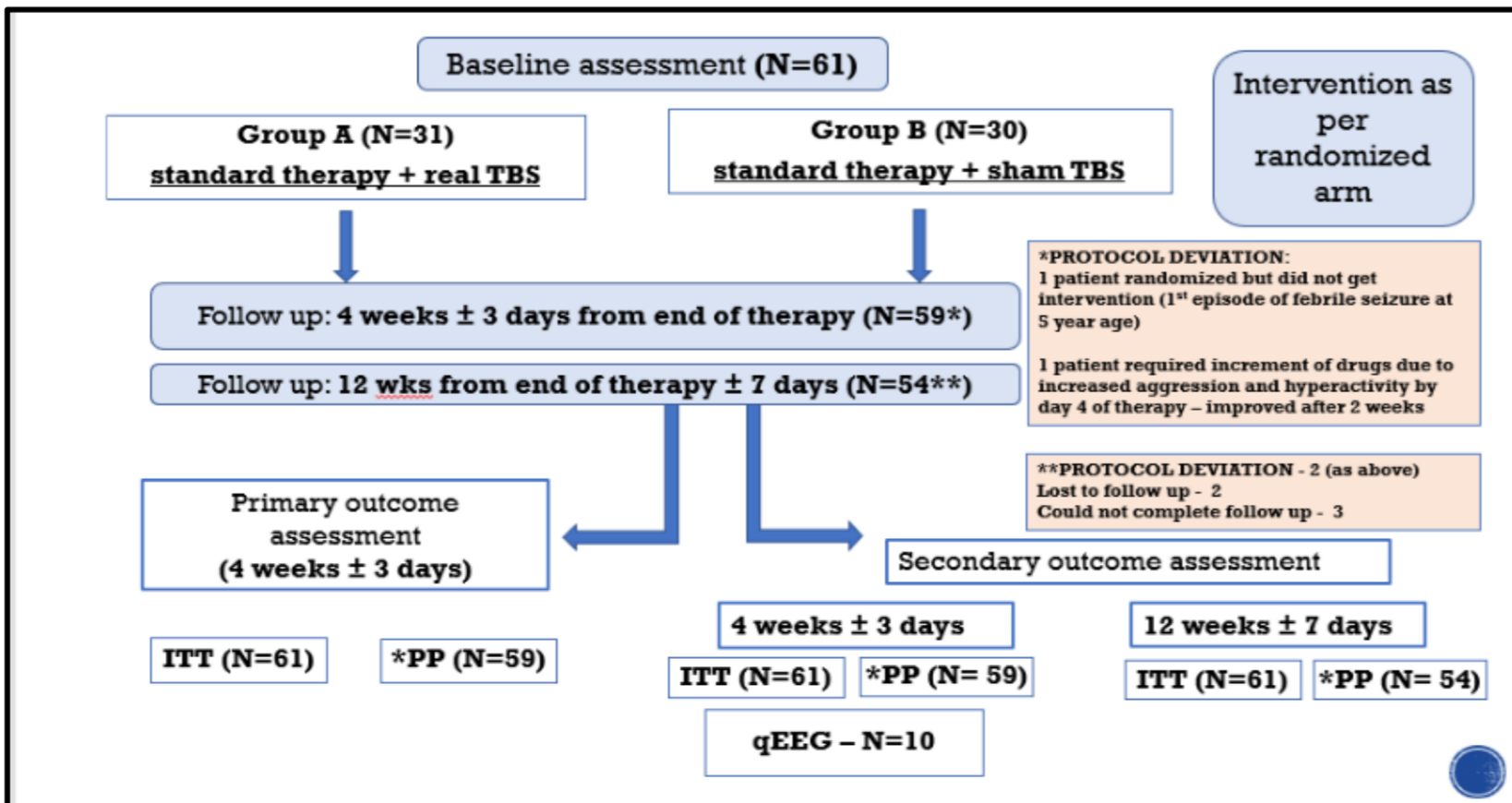
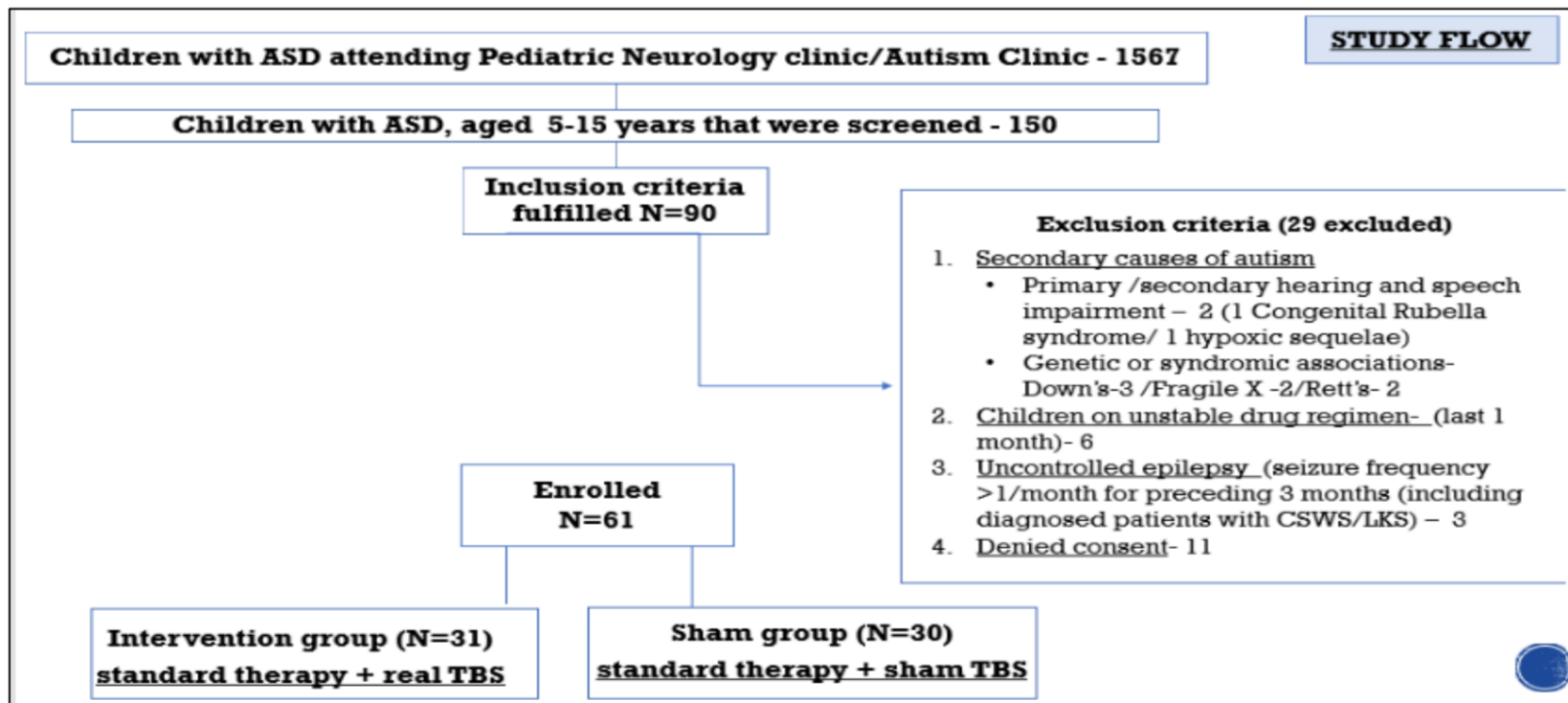
TBS Parameter	Set value
Frequency	3 pulses at 50 Hz- 1 BURST
Interburst interval	200ms (Bursts at 5Hz)
Train	40sec on-20 sec off – 1 train
No of trains	5 such trains in each session Pause of 1 minute in between 2 trains
Intensity	100% of RMT of dominant side
Site of stimulation	Dorsolateral prefrontal cortex of non-dominant side
Co-ordinates for locating stimulus site	Site of F3 electrode (BeamF3 method)
Type of coil	MCF-B65
Duration	10 minutes



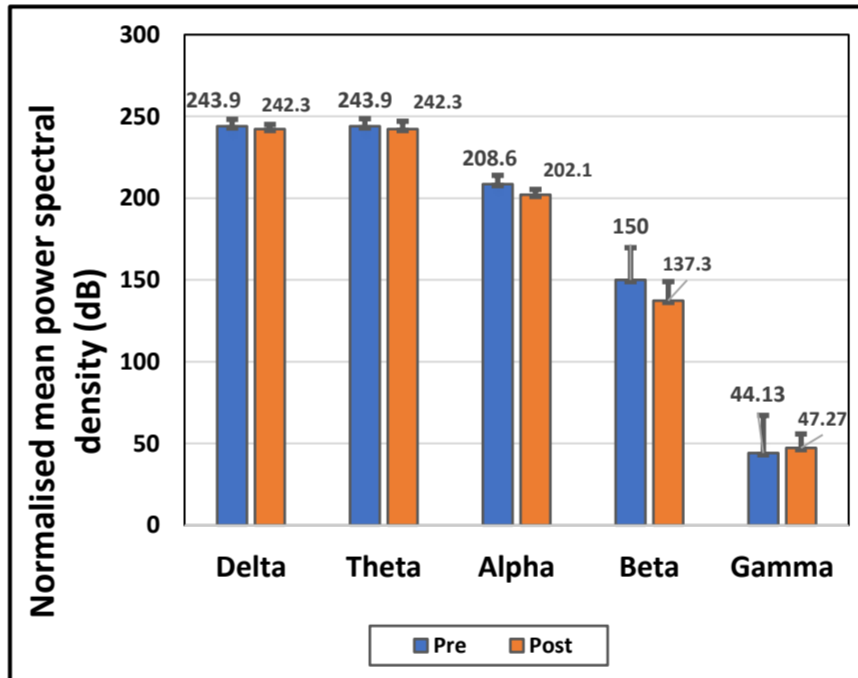
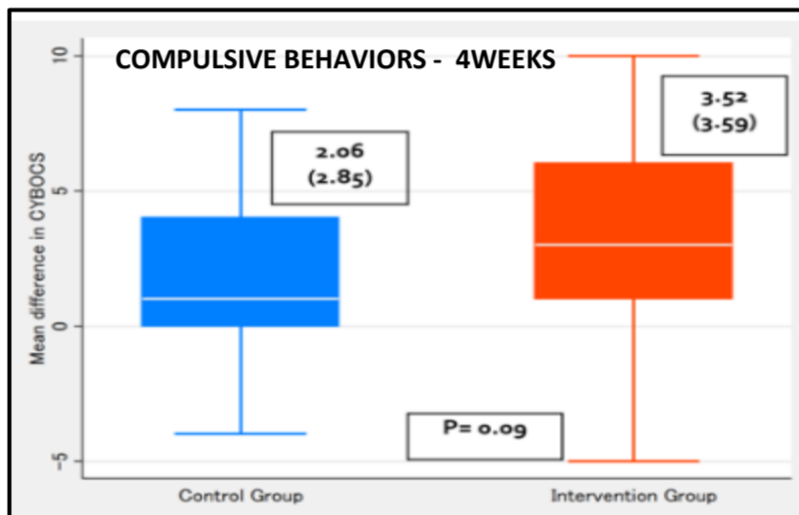
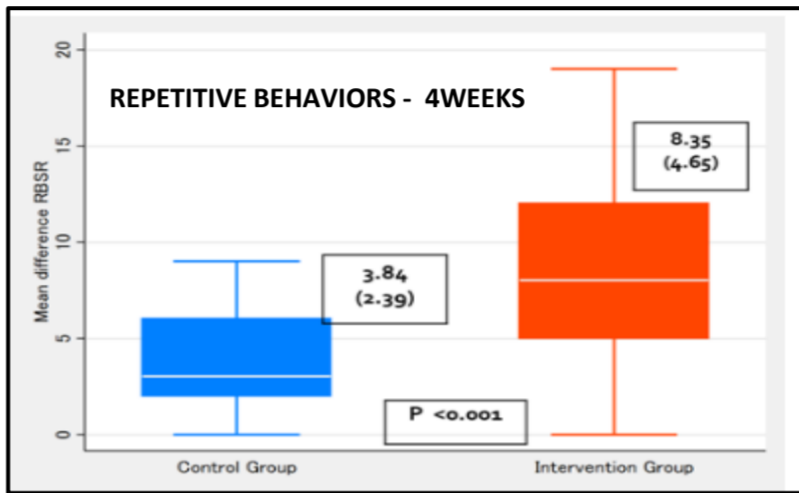
Intervention set up



MCF-B65 Magventure
Magoption coil

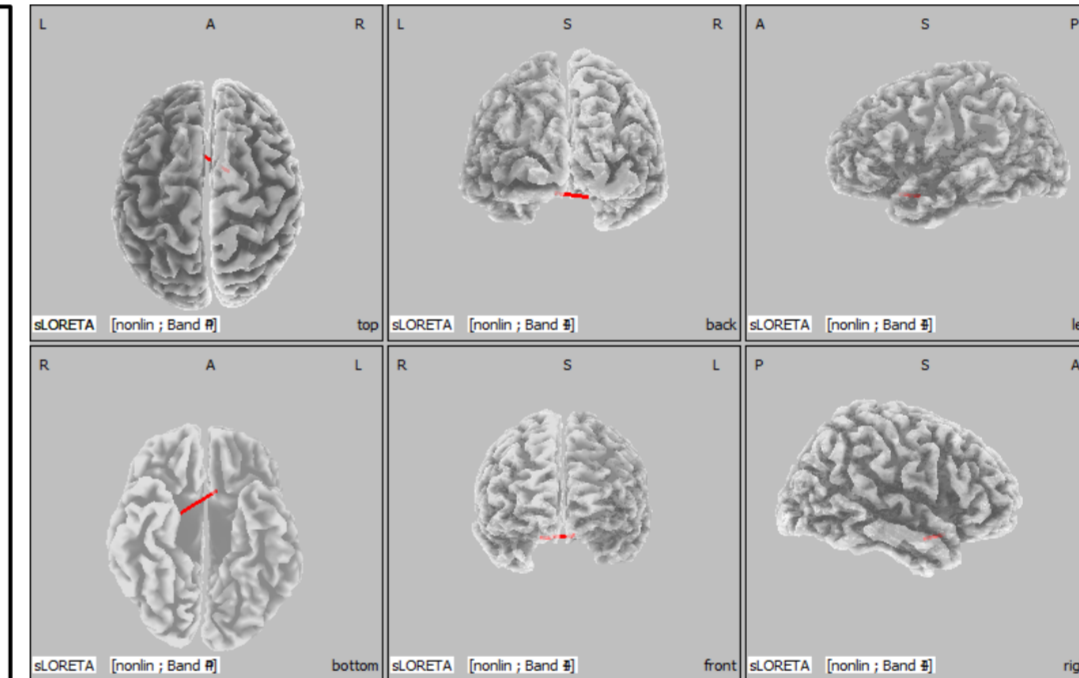


Results



	Intention to treat (N=61)		P-value
Parameter	Intervention group (N=31)	Sham group (N=30)	
REPETITIVE BEHAVIORS - 4 WEEKS			
RBS-R *	8.35 (4.65)	3.84 (2.39)	<0.001
COMPULSIVE BEHAVIORS – 4 WEEKS			
CY-BOCS*	3.52 (3.59)	2.06 (2.85)	<0.001

CY-BOCS, CARS-2 and SRS-2, Time to Stroop and Wisconsin card sorting, did not show significant changes.



	Intention to treat (N=61)		P-value
Parameter	Intervention group (N=31)	Sham group (N=30)	
REPETITIVE BEHAVIORS - 12WEEKS			
RBS-R*	10.71 (5.49)	6.37 (2.39)	<0.001
COMPULSIVE BEHAVIORS - 12WEEKS			
CY-BOCS*	5.52 (4.14)	3.57 (2.89)	0.067
PARENT REPORTED QUALITY OF LIFE (PedsQL) – 4 WEEK			
PedsQL *	6.35 (2.37)	2.97 (1.12)	<0.001
PARENT REPORTED QUALITY OF LIFE (PedsQL) – 12 WEEKS			
PedsQL *	8.19 (2.87)	4.67 (1.47)	<0.001

Tables show differences in mean score of the scale used

- TBS was well tolerated in the study population. Adverse event rate was 28.1% in intervention arm and 5.7% in sham arm. No serious adverse events were reported.
- qEEG spectral coherence demonstrated increased beta band coherence between Limbic and Frontal lobes but spectral power did not change post TBS.

STRENGTHS

- Uniform method for locating site for therapy ensured at all sessions
- Standard therapy compliance ensured via weekly telephonic calls
- 1 month follow up achieved in all subjects who received therapy
- Both parent and psychologist evaluated scores used as outcome measures - blinded to treatment arm
- Attempt to explore changes in qEEG in ASD children pre and post TMS therapy

LIMITATIONS

- Surface localization for DLPFC
- Severity heterogenous hence response may not be applicable to all subsets of ASD
- Parent reported parameters used to assess behavioral parameters
- Stroop, WSCT and qEEG done in subset (IQ>70) and the results may not be generalizable

Conclusion

- TBS may be used as an upcoming non-invasive neuromodulating modality in treatment of children with ASD, especially with significant repetitive behaviors. Role of qEEG to detect changes post TBS may need further exploration. Determinants of response to treatment may need evaluation in further studies.

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