Transcranial Magnetic Stimulation is Safe in Pediatric Clinical Populations

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Introduction

The safety of TMS has been previously evaluated in healthy volunteers and clinical adult populations[1-3]. We sought to fill the gap in safety of TMS functional mapping in a clinical, pediatric cohort.

- Thus far, the safety of TMS as used in functional mapping has been reported in few studies in healthy and clinical populations[1-3].
- With respect to safety of TMS in children, previous studies have shown that TMS is a safe procedure and does not cause harm to children[4,5].
- Prior to this report, there are no reports on the safety of TMS in children with epilepsy or brain tumor requiring presurgical functional mapping.
- More safety reporting is needed to provide an accurate picture of the safety of TMS, especially when it comes to pediatric uses and protocols[6,7].

Significance

This study demonstrates the safety of TMS functional mapping in patients with refractory epilepsy, brain tumor and cranial metal and fills a gap in knowledge for TMS safety in pediatric clinical population.

- A large single center safety review of TMS motor and language mapping in a clinical cohort comprising of 80% children.
- The majority of adverse events were benign and transient; the most severe adverse events were seizures that could not be conclusively attributed to TMS.
- TMS is safe in a pediatric cohort with refractory epilepsy, brain tumor, and the presence of cranial metal.
- Improved record keeping and additional safety measures in pediatric TMS procedures are recommended.

Method

Retrospective Chart Review
TMS motor and language mapping studies in children with epilepsy or brain tumor were evaluated for adverse events and safety of TMS and in patients with cranial metal.

- Approved by both the IRB at the University of Tennessee Health Science Center and Le Bonheur Children's Hospital.
- Information extracted:
  - Clinical, anthropometrics and demographics
  - TMS parameters
  - Written records & session videos assessed and compared to clinical video EEG recordings by a board certified Pediatric Epileptologist to ensure accuracy and consistency in seizure reporting
- 500 TMS studies → August 2012 - June 2020
  - 429 individual patients

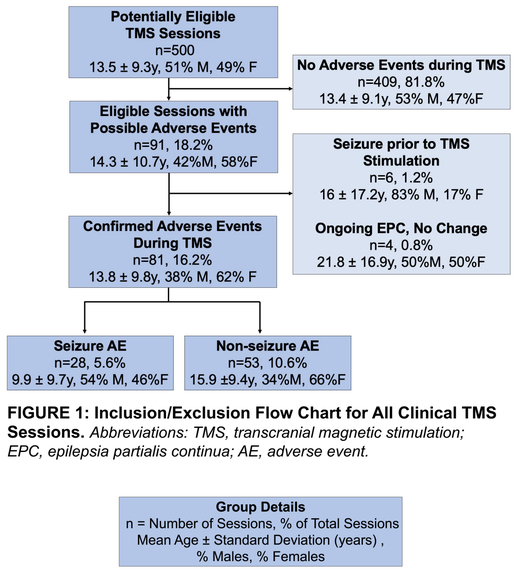

FIGURE 1: Inclusion/Exclusion Flow Chart for All Clinical TMS Sessions. *Abbreviations: TMS, transcranial magnetic stimulation; EPC, epilepsia partialis continua; AE, adverse event.*

Results

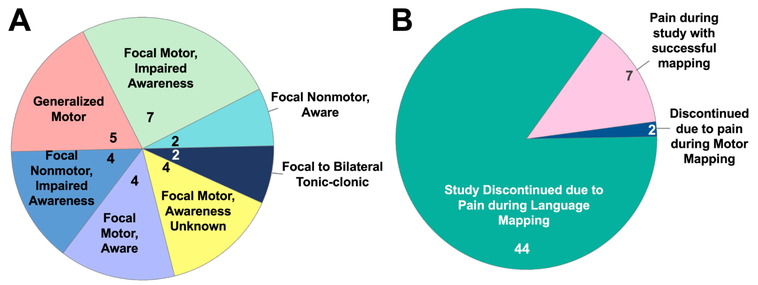

FIGURE 2: Total Clinical TMS Cohort with details on Adverse Events Cohorts.
A) Seizure types listed here are what occurred during the TMS studies. There were 2 Generalized tonic-clonic seizures requiring the use of rescue medications; B) The non-seizure adverse events are comprised of language studies that were discontinued due to pain, studies that were successful but resting motor threshold could not be assessed due to pain at stimulation site, and two studies where motor mapping was discontinued due to pain.

- 28 sessions had seizure during or after TMS
- 53 experienced pain during stimulation
- 276 patients with cranial metal & successful TMS study

All TMS-associated seizures:
- Consistent with normal seizure semiology, duration, & recovery
- Determined to be coincidental, as they most likely would have happened regardless of stimulation

TABLE 1: Demographics.
Diagnoses and Average ASM per patient for total cohort and adverse event cohorts, seizure group and non-seizure group. Bolded values indicate a significant results for student t-Tests (p = <0.05).

Group # of TMS Sessions	Total Cohort n = 500		Seizure AE Cohort n = 28		Non-Seizure AE Cohort n = 53	
Diagnosis	# of Patients	% of Total Cohort	# of Patients	% of Seizure AE Cohort	# of Patients	% of Non-seizure AE Cohort
Epilepsy	399	80%	27	96%	38	72%
Focal/generalized Epilepsy	178	36%	11	39%	16	30%
Epilepsy Secondary to Brain Malformation	80	16%	3	11%	8	15%
Epilepsy Secondary to Stroke/hemorrhage	42	8%	1	4%	5	9%
Epilepsy Secondary to TSC	32	6%	5	18%	3	6%
Epilepsy Secondary to Prior Brain Tumor	30	6%	3	11%	2	4%
Epilepsy Secondary to Infection	15	3%	3	11%	3	6%
Epilepsy Secondary to TBI	12	2%	1	34%	1	2%
Epilepsy Secondary to Other Causes	10	2%	0	0%	0	0%
Newly Diagnosed Brain Tumor	92	18%	1	4%	13	25%
Functional Neurological Disorder	7	1%	0	0%	2	4%
Non-epileptic Neurological Disorders	2	<0.05%	0	0%	0	0%
Average (± S.D.) # of ASM per patient	1.92 ± 1.14		**2.46 ± 1.04***		1.81 ± 1.08	

Abbreviations: TMS, transcranial magnetic stimulation; AE, adverse event; TSC, Tuberous sclerosis complex; TBI, traumatic brain injury; ASM, anti-seizure medication; S.D. standard deviation.

Conclusions

Despite all seizures being consistent with typical semiology, we are reporting these as TMS-associated seizures and the risk of having a seizure associated with TMS in our cohort was 5.6%. While this may at first glance appear to be higher than previous reports, we believe that given the nature of our cohort and our reporting protocol, it is not alarming.

Most of the patients who had TMS-associated seizure had a history of having daily seizures or multiple-daily seizures. Furthermore 10 patients in this group were children under 3 years of age with significant refractory epilepsy syndromes seeking treatment.

In order to further improve the safety of TMS studies, standardized screening and adverse event documentation is urgently needed for pediatric clinical TMS sessions.

Most TMS-related adverse events were benign and transient; the most serious safety events were seizures that could not be conclusively attributed to TMS. However, useful mapping results were obtained in almost all patients. Presence of cranial metal did not adversely affect TMS mapping. We show that TMS functional mapping is safe in clinical pediatric cohort.

Acknowledgments

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