

# A Masked, Controlled Trial of Median Nerve Stimulation for Tourette Syndrome

Amanda L. Arbuckle; Emily C. Bihun; David Song; Jonathan M. Koller; Ann Iverson, Keisuke Ueda, Kevin J. Black

Median nerve stimulation for Tourette syndrome is well tolerated. Some patients have dramatic improvement. The mechanism of improvement is unclear.



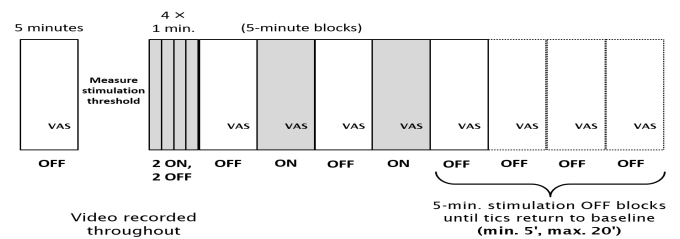
Download the full study protocol



Questions to kevin@WUSTL.edu

## INTRO

- In mid-2020, the Stephen Jackson lab published intriguing results showing that rhythmic—but not arrhythmic—stimulation of the median nerve (MNS) entrained EEG power at the same frequency. Rhythmic MNS reduced tic severity in Tourette syndrome (TS) and entrainment was proposed as the mechanism for this reduction.
- However, no control condition was tested and stimulation blocks lasted only one minute, making it difficult to rule out a placebo effect or test whether entrainment was the mechanism responsible for the reduction.
- Our hypotheses:** (1) tic improvement is specific to rhythmic stimulation, which alone entrained cortical activity, and (2) the benefit lasts after MNS ends.



## METHODS

- TS, age 15-64, N = 32. Two MNS visits, 1 rhythmic, 1 arrhythmic, random order, both at 12Hz, no EEG produced for arrhythmic
- Subjects & staff blind to order; video raters also blind to block order and to stimulation on vs. off

## RESULTS

- Discomfort was rated none or minimal on 58 of 64 visits
- Masking was effective

### Selected comments by participants

- "This is literally the first time in 50 years I felt free of the need to tic."
- "I had at least one of my tics throughout the whole time, but that was the least number amount of tics and the least frequency my tics have been throughout my entire life."

	Rhythmic	Arrhythmic
CGI-I Participant Rating	2.7 ± 1.0	2.5 ± 1.2
CGI-I Investigator Rating	2.4 ± 0.9	2.6 ± 1.0

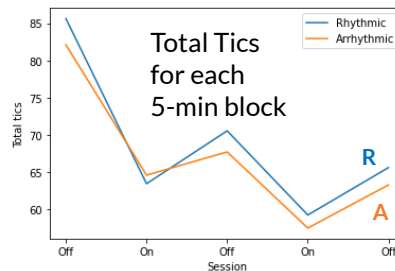
	Visit 1	Visit 2
CGI-I Participant Rating	2.6 ± 0.98	2.6 ± 1.21
CGI-I Investigator Rating	2.6 ± 0.84	2.4 ± 1.07

2 = Much improved, 3 = Minimally improved

### CGI Efficacy Index (participant) Rhythmic

Therapeutic effect	Side effects			
	None	Do not significantly interfere with patient's functioning	Significantly interfere with patient's functioning	Outweigh therapeutic effect
Marked — Vast improvement. Complete or nearly complete remission of all symptoms	3	3	2	
Moderate — Decided improvement. Partial remission of symptoms	8	4	2	
Minimal — Slight improvement which doesn't alter status of care of patient	3	3	1	
Unchanged or worse	1	3	1	

Therapeutic effect	Side effects			
	None	Do not significantly interfere with patient's functioning	Significantly interfere with patient's functioning	Outweigh therapeutic effect
Marked — Vast improvement. Complete or nearly complete remission of all symptoms	4	3	1	
Moderate — Decided improvement. Partial remission of symptoms	4	10	1	
Minimal — Slight improvement which doesn't alter status of care of patient	1	3		
Unchanged or worse	1	3		



### Participant Ratings

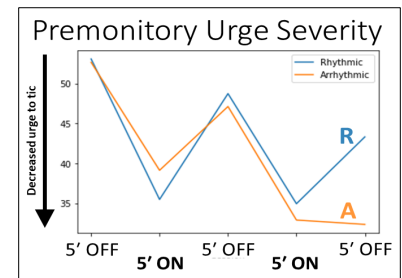
- 13 A>R Stimulation, 6 R>A stimulation
- 18 "Decided improvement, partial remission" (at least one visit)
- 11 "Complete or nearly complete remission of symptoms"
- 29 "Very Much Improved" or "Much Improved"

### Investigator Ratings

- 10 A>R, 9 R>A
- 29 "Very Much Improved" or "Much Improved"

### Participants: Demographics

Descriptor	Mean ± SD (n=32)
Age	34.0 ± 16.5 (15-64)
Sex	21M, 11F
Handedness	29 R, 3 L
YGTS Total tic score	25.8 ± 7.9
YGTS Motor	16.0 ± 3.5
YGTS Phonic	9.8 ± 5.6
YGTS Impairment	19.5 ± 15.5
CY-BOCS total	6.3 ± 6.0
DCI	60.6 ± 19.9
SRS	53.2 ± 11.3
Marked distress or impairment, past week	18



Urge severity decreased during stimulation blocks (both rhythmic and arrhythmic)



### Participant Blindedness Data (p=.01)

- 20/32 or 62.5% of visits were guessed correctly to be rhythmic
  - 3 of the 20 correct guesses were perceived as "certain", 6 as "very likely", 7 as "hunch", and 3 as "pure guess".
  - 9/32 or 28.1% of visits were guessed correctly to be arrhythmic
  - 1 of the 9 correct guesses was "certain", 5 were "very likely", 2 were "hunches", and 1 was "pure guess".
- Investigator Blindedness data (p=.45)
- 19/32 or 59.4% of visits were guessed correctly to be rhythmic
  - 12 of the 19 were "very likely", 6 were "hunch", and 1 was "pure guess".
  - 16/32 or 50.0% of visits were guessed correctly to be arrhythmic
  - 4 of the 16 guessed correctly were "very likely", 11 were "hunch", and 1 was "pure guess".

## DISCUSSION

- MNS appears to be well tolerated.
- Some participants had remarkable symptom improvement.
- Rhythmic stimulation does NOT outperform arrhythmic stimulation. Thus, induction of mu-band EEG power in primary motor cortex is unlikely to explain any benefits of MNS on tics.