Connectivity of the centromedian nucleus of the thalamus: Insights from brain stimulation and intracranial electroencephalography

Karim Mithani, MD MEng[1, 2]; Simeon M. Wong MASc[2]; George M. Ibrahim, MD PhD[1, 2]

[1] Division of Neurosurgery, Hospital for Sick Children, Toronto, Canada
[2] Institute of Biomedical Engineering, University of Toronto, Toronto, Canada

At-a-glance

We analyzed rare intracranial electroencephalographic recordings from children undergoing epilepsy monitoring to map the connectivity of the centromedian nucleus of the thalamus. This represents a pivotal advancement towards developing precise, targeted neurotherapies for the treatment of drug-resistant epilepsy in children.

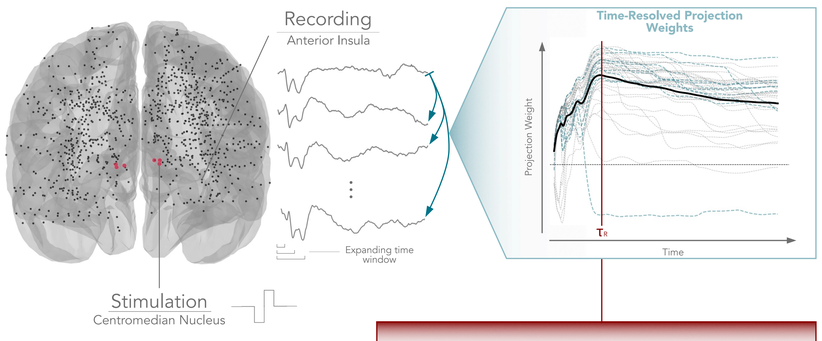
BACKGROUND

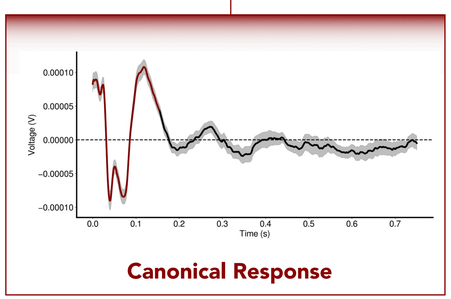
The bilaterally paired **centromedian nuclei of the thalamus (CM)** are critical nodes of the mammalian brain, with extensive projections subserving a range of neurocognitive functions.

In rodents and non-human primates, CM deep brain stimulation was found to result in in widespread cortical desychnronization, leading to its eventual use as a **potential treatment for drug-resistant epilepsy.**

Despite the increasing use of **CM deep brain stimulation (DBS)** to treat drug-resistant epilepsy, **the connectivity of the CM in humans remains largely unknown.**

METHODS



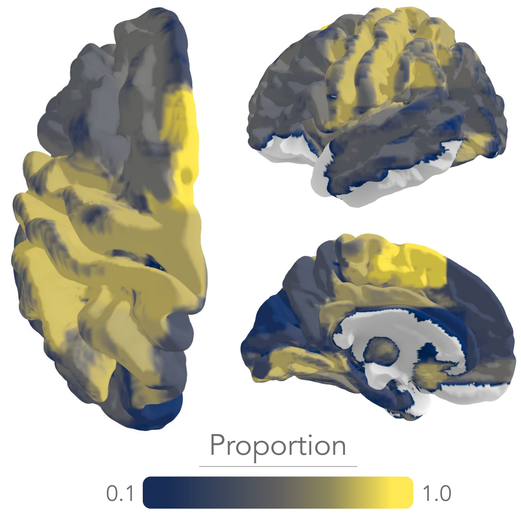


N = 6 children wtih drug-resistant epilepsy

Canonical response parameterization
(Miller et al., 2024)

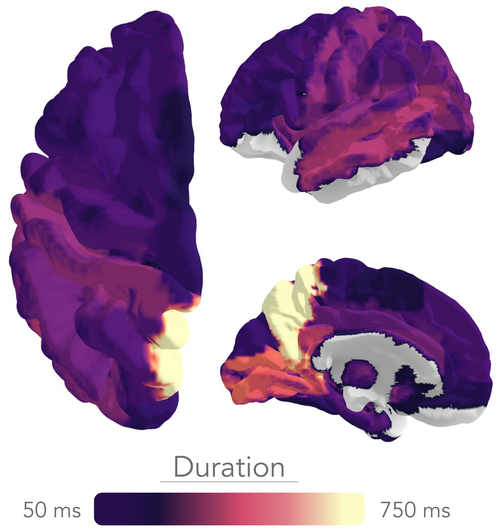
RESULTS

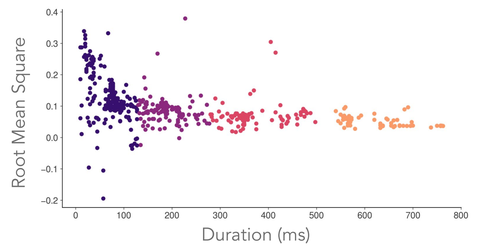
1 Centromedian nucleus stimulation engages a large-scale, distributed network, centered on the Rolandic cortex cortically and the dorsal striatum subcortically

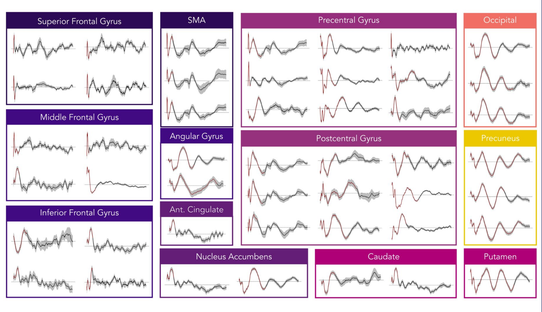


Region	Count	Proportion Significant
Supplementary Motor Area	7	100%
Supramarginal gyrus	14	86%
Postcentral Gyrus	60	83%
Precentral Gyrus	61	80%
Middle Cingulate Gyrus	51	75%
Posterior Cingulate Gyrus	16	70%
Striatum	28	68%
Fusiform Gyrus	9	56%
Insula	109	53%
Lateral Prefrontal Cortex	62	50%
Lateral Temporal Cortex	53	48%
Hippocampus	19	26%
Anterior Cingulate Gyrus	13	23%

2 The centromedian nucleus engages dissociable sensorimotor, limbic, and associative subnetworks based on the duration of evoked activity







DISCUSSION

Despite being central to many critical cognitive and behavioural functions, **the connectivity of the CM in humans has remained largely unexplored.**

Using **intracranial electroencephalography** and ***in vivo* brain stimulation**, we **causally mapped** the connectivity of the CM in children with drug-resistant epilepsy.

CM-DBS may exert its effects by modulating activity within these circuits. Ongoing efforts are directed at investigating **whether seizure propagation to the CM occurs through this network**, and whether **selective engagement** of this network is associated with **outcomes after DBS.**

CONCLUSION

CM stimulation engages a large-scale cortico-subcortical network, with dissociable sensorimotor, limbic, and associative subnetworks. This widespread connectivity makes it a suitable target for stimulation-based treatments of drug-resistant epilepsy, and may underlie its diverse role in mediating cognition and behaviour in humans.

REFERENCES & ACKNOWLEDGMENTS

Miller KJ, Müller KR, Valencia GO, et al. Canonical Response Parameterization: Quantifying the structure of responses to single-pulse intracranial electrical brain stimulation. PLoS Comput Biol. 2023;19(5):e1011105. doi:10.1371/journal.pcbi.1011105

Google Scholar
LinkedIn
@KarimMithaniMD
karim.mithani@utoronto.ca