

Reduced complexity in stroke with motor deficit and the role of VNS therapy

Authors: Francesco Sammartino*, Vibhor Krishna*, Erin Woodburn+, Marcia Bockbrader+

Affiliations: * Department of Neurosurgery / + Department of Physical Medicine and Rehabilitation



THE OHIO STATE
UNIVERSITY

WEXNER MEDICAL CENTER

Background

A pivotal phase III trial (VNS-REHAB, NCT03131960) is underway to evaluate efficacy of active vs. sham VNS during rehabilitation after stroke. However, the stroke population is heterogeneous; a functional magnetic resonance imaging (fMRI)-based metric of motor impairment may help identify patients with the best potential for recovery.

We aim to evaluate fMRI-based Brain Entropy Mapping (BEN) as an imaging correlate of upper limb motor impairment post-stroke, defined by Fugl-Meyer Assessment-Upper Extremity (FMA-UE) score.

Design

Five stroke patients (3 sham, 2 VNS) were recruited (mean age 58.4/SD) along with 5 healthy controls (mean age 59.0/SD 3.9). Baseline structural and resting state fMRI were obtained for both groups. Volume of stroke lesions and BEN (SampEn; Wang et al., 2014) was calculated. FMA-UE was acquired in the stroke group at baseline and after 6 weeks of treatment.

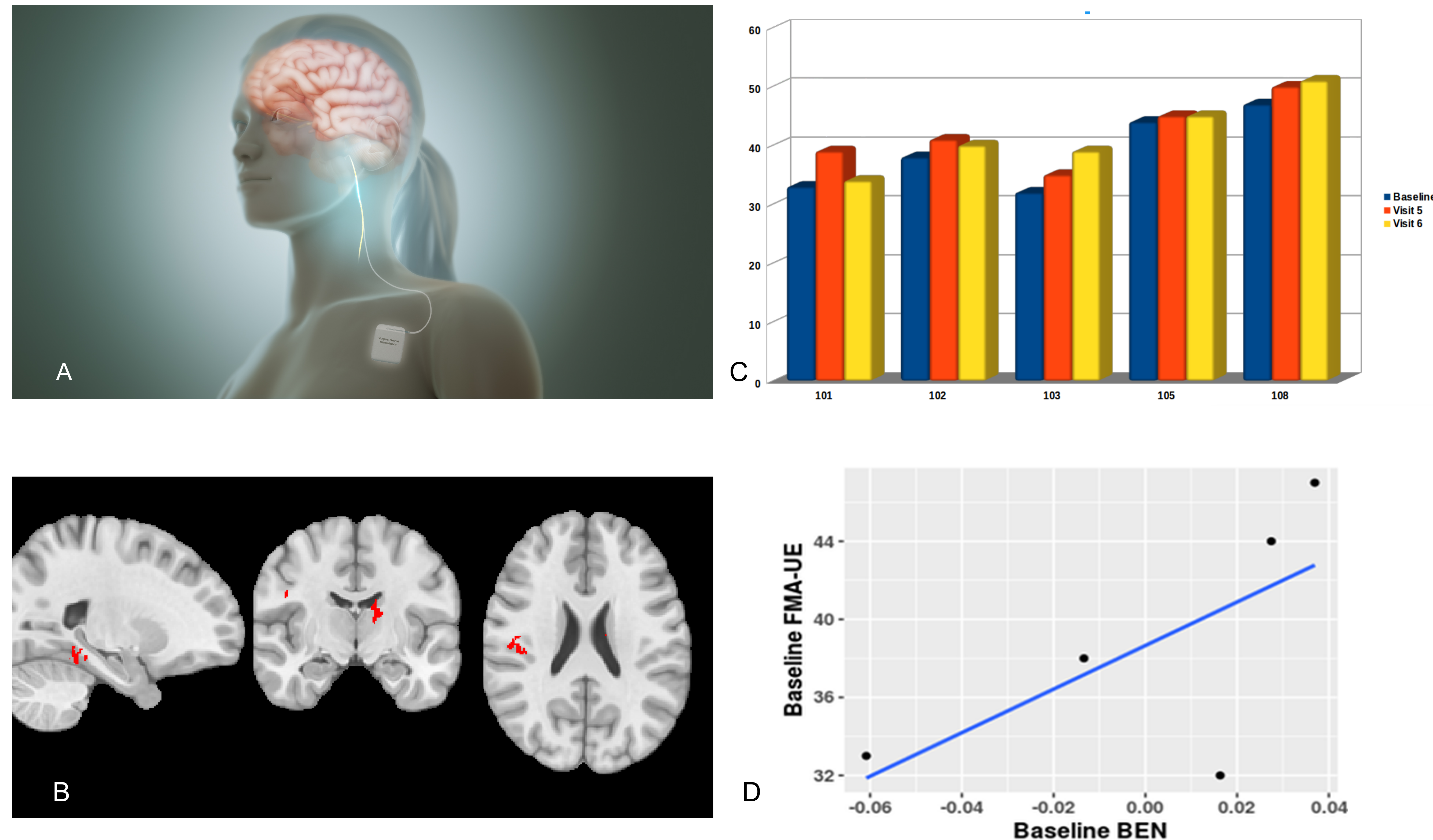


Figure A: Depiction of a vagal nerve stimulator (VNS) implant. B: Significant clusters with decreased entropy between stroke patients and controls. C: FMA-UE scores for the study participants at the different visits - 101&108 are in the active VNS group. D: Correlation between baseline BEN in the precentral gyrus cluster and baseline FMA-UE scores in the stroke patients ($r=0.66$).

References:

- Liang, L., Hu, R., Luo, X., Feng, B., Long, W., & Song, R. (2020). Reduced complexity in stroke with motor deficits: a resting-state fMRI study. *Neuroscience*.
- Kimberley, T. J., Khandekar, G., & Borich, M. (2008). fMRI reliability in subjects with stroke. *Experimental brain research*, 186(1), 183-190.
- Pivotal Study of VNS During Rehab After Stroke (VNS-REHAB) (VNS-REHAB) : <https://clinicaltrials.gov/ct2/show/NCT03131960>.
- Saenger, V. M., Ponce-Alvarez, A., Adhikari, M., Hagmann, P., Deco, G., & Corbetta, M. (2018). Linking entropy at rest with the underlying structural connectivity in the healthy and lesioned brain. *Cerebral Cortex*, 28(8), 2948-2958.

Results

Mean stroke lesion volume for participants was 5.2 ± 8.7 cc. Compared to controls, stroke patients had decreased entropy in the contra-lateral motor cortex, ipsilateral caudate and para-hippocampal gyrus (largest effect size Cohen $d=5.5$, range: 2.3-8.7; t-test, 5000 permutations, cluster-corrected $p=0.048$). Imaging (SampEN for right motor cortex cluster) and functional (FMA-UE) metrics of motor impairment were significantly correlated ($r=0.66$, p -value=0.12). Participants randomized to active rather than sham VNS had a larger gain in FMA-UE after 6 weeks of rehabilitation (mean $12.2 \pm 8.3\%$ vs. 3.3 ± 4.0 , respectively).

Conclusion

Brain entropy is a promising imaging metric of upper limb motor impairment in stroke; it is decreased in stroke patients and it shows association with FMA-UE scores. Longitudinal studies with larger sample size are required in order to assess its value in VNS therapy coupled with rehabilitation.