PROJECT

Supervisor:	DAVIDE FOLLONI
Title:	**From Network Gradients to Causality: Non-invasive Ultrasound Modulation of the Brain's Macroscale Architecture and Deep Brain Connectivity**
Curriculum:	____
Link to the personal page of the University or relevant hospital site website:	Website under development by uniSR. See: https://scholar.google.com/citations?user=1VeU0HMAAAAJ&hl=it and https://www.linkedin.com/in/davide-folloni-08130a73/

Description of the Project (max 3,000 characters including spaces)

Background/gap of knowledge

Recent advances in neuroscience show that the brain is organised in macroscale gradients rather than discrete regions or networks (Mars et al., 2018). At the top of the functional and topographical hierarchy in cognition, the sensory-transmodal and the default-mode gradients capture systematic transitions in microstructure, connectivity and intrinsic timescales, and are conserved across species and modalities (Margulies et al., 2016; Paquola et al., 2025). Despite their explanatory power, the understanding of these gradients remains correlational and it is unknown whether (1) they constrain neural dynamics and behaviour or whether (2) they simply summarise emergent properties of brain networks. To date, no study has directly manipulated their deep brain hubs in humans in the context of decision-making or mood and tested their functional relevance for mental health.

Rationale and hypothesis

Over the past years, we have developed focused transcranial ultrasound stimulation (TUS) protocols able to non-invasively modulate at a millimetric resolution both cortical and deep brain hubs and networks (Folloni, 2026; 2022; 2021; 2019). This PhD project leverages TUS and resting-state functional Magnetic Resonance Imaging (rs-fMRI) to move network gradients from description to causal testing to use them as future clinical biomarkers. The hypothesis is that macroscale gradients constitute causal axes of information integration: perturbing neural activity at distinct positions along a gradient will induce predictable, system-wide reconfigurations of functional connectivity, neural dynamics and cognition aligned with the intrinsic gradient architecture.

Objectives and specific aims

The overall objective is to causally test the role of macroscale brain gradients in shaping neural dynamics:

Aim 1: Estimate individual functional connectivity gradients from human rs-fMRI and identify the effects of deep brain TUS on unimodal and transmodal hubs.

Aim 2: Quantify changes in whole-brain functional connectivity, gradient geometry and activity propagation along gradient axes.

Aim 3: Assess behavioural/autonomic effects of gradient-specific neuromodulation using ultrasounds.

Expected outcomes

This project will provide novel and innovative causal evidence linking macroscale brain gradients to neural dynamics and cognition in deep brain circuits. You will learn to collect and analyse data from both TUS and fMRI. Expected outcomes include the identification of the neuromodulatory effects of brain gradients on the macroscale brain network organisation. These results will determine causal gradient-sensitive markers of network hierarchies and establish a network framework for brain organisation-guided neuromodulation. These findings will advance basic theories of brain organisation and inform translational strategies for disorders characterised by disrupted large-scale gradient architecture.

Skills that the student should acquire (max. 600 characters including spaces):

- Coding & stats skills (Python/Matlab/R)
- Transcranial Ultrasound Stimulation
- Neuroimaging design, data collection and analysis
- Autonomic measurements data collection and analysis
- Computational modeling & advanced neural network analysis
- Scientific curiosity, teamwork and project management
- Manuscript and grant writing
- Translational skills in neuroscience

References (max. 15)

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4) Folloni, D., Sallet, J., Khrapitchev, A. A., Sibson, N., Verhagen, L., & Mars, R. B. (2019). Dichotomous organization of amygdala/temporal-prefrontal bundles in both humans and monkeys. eLife, 8. https://doi.org/10.7554/eLife.47175

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6) Margulies, D. S., Ghosh, S. S., Goulas, A., Falkiewicz, M., Huntenburg, J. M., Langs, G., Bezgin, G., Eickhoff, S. B., Castellanos, F. X., Petrides, M., Jefferies, E., & Smallwood, J. (2016). Situating the default-mode network along a principal gradient of macroscale cortical organization. Proceedings of the National Academy of Sciences of the United States of America, 113(44), 12574–12579. https://doi.org/10.1073/pnas.1608282113

7) Mars, R. B., Sotiropoulos, S. N., Passingham, R. E., Sallet, J., Verhagen, L., Khrapitchev, A. A., Sibson, N., & Jbabdi, S. (2018). Whole brain comparative anatomy using connectivity blueprints. eLife, 7. https://doi.org/10.7554/eLife.35237