FUSIMICE: Ultrafast Functional Ultrasound (fUS) Imaging for Highly-Resolved Targeted Mapping of Functional Connectivity in the Awake Mouse Brain

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Abstract

The mouse brain provides unique opportunities in brain connectivity mapping, both to understand how the genotype regulates the phenotype and to understand the dynamics and pharmacological regulation of brain connectivity in well-controlled and highly-reproducible experimental setups. Recently we have developed a novel paradigm of functional connectivity mapping - Ultrafast Functional Ultrasound or fUS (Osmanski et al., Nature Communications, 2014). Through achieving parallel measurement of functional parameters with sensitivity, spatiotemporal resolution and operating simplicity unmatched by current imaging modalities, fUS may open access to previously unexplored aspects of brain function. In particular, fUS may be a ground-breaking novel method mapping not only functional connectivity, but coupled to optogenetics, also mapping effective connectivity in awake mice. This could vastly accelerate the adaptation of connectivity-based experimental approaches in neuroscience research environments. For the validation of these promises, here we propose a complementary European research network to validate the fUS technique for targeted mapping of the mouse brain.

First, the French partners (1&2) will adapt the fUS technique for minimally-invasive whole-brain mapping in awake mice, by using a motorized 2D ultra-light prototype ultrasound probe. Direct real-time 3D mapping will also be developed by using a 2D-matrix prototype probe. Typical experiments will aim to map major resting-state networks, already identified in human (such as the Default Mode Network), in awake resting mice. By using mouse fMRI equipment, the Belgian partner (3) will contribute to the development and validation of analytical tools for the interpretation of fUS connectivity data. We will compare the performance of fUS- versus the standard fMRI-based mapping approaches on the same animal models and using similar analytical approaches. This will provide insights into the relative strengths and weaknesses of the fUS method. The Hungarian partner (4) will provide fine-grained connectivity data to verify well-defined sets of connections identified by fUS. Next, using proof-of-concept optogenetic experiments, partners 1 and 4 will induce targeted changes in specific thalamocortical networks, and record the changes in behavior, EEG activity and functional brain connectivity in parallel. Finally, partners 1 and 3 will aim to map alterations in functional connectivity in mouse models of neurological diseases.

As a result, this project will produce new functional insights that will complete existing data sets on the mouse brain structure and facilitate mouse-human comparisons. Hopefully, the tools developed in this project will be the base of future user-friendly, cost-effective bench-top based fUS systems, optimized for the mapping of functional connectivity of the mouse brain, and ready-to-use in a standard neuroscience research lab, both in academic and industrial research environments.

Consortium

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