Webinar Q&A Report

Functional Ultrasound Imaging in Pain and Pharmacology

Questions in this Q&A Report were submitted during the live webinar, <u>Functional Ultrasound</u> <u>Imaging in Pain and Pharmacology</u>.

Answers have been provided by:

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Could you comment a little bit about the pros and cons of using fMRI and fUS to look at brain connectivity? What benefits does the fUS offer compared to fMRI?

B. Vidal: I would say that fUS compensates a lot of fMRI drawbacks for preclinical imaging. It has a higher resolution and sensitivity and is therefore more suited to study functional connectivity of small regions. It is also much easier to study functional connectivity in awake animals using fUS, even in freely moving animals. Another asset is that it is more versatile (easier to use other devices at the same time, for instance EEG, as it does not require a magnetic field).

The main drawback is that it is mostly optimized for 2D imaging for now. The probe can be moved among several slices but it is currently difficult to cover the full brain volume as quickly as fMRI.

Can we perform multimodal analyses, for example combining fUS with EEG/electrophysiology/optogenetics?

S. Pezet: Yes, of course. This was done previously in the following publications:

- EEG/ LFP and fUS: <u>Sieu et al., 2015</u>; <u>Urban et al., 2015</u>; <u>Bergel et al., 2018</u>, <u>2020</u>; <u>Macé et al., 2018</u>.
- Optogenetics and fUS: <u>Rungta et al., 2017</u>; <u>Brunner et al., 2020</u>.

Could you comment on how the signal-to-noise-ratio (SNR) for pharmaco-fUS varies with depth in mouse brain? Is it reliable for deep brain structures?

B. Vidal: fUS is reliable to study the deepest brain structures in mouse, although with transcranial imaging there is some SNR variability among individuals. If the question is specifically focused on deep regions, I would recommend doing a cranial window, which has been previously done in other publications for mouse or rat.

Can fUS be used to study other organ systems like kidneys, liver, or lungs?

Iconeus: Ultrafast Ultrasound imaging can be applied to any soft tissue such as the Kidney or the Liver. However, it is strongly affected by gas cavities such as the lung.

Thanks for this very interesting webinar. On the arthritis study, I was wondering why you chose to select 7 brain states. Why not fewer or more?

S. Pezet: You are welcome. Thank you for your interest in this webinar.

We performed this part of the study with J Sitt from the ICM in Paris, who has extensive experience in the analysis of dynamic signals in human subjects. To his experience (but nothing so scientific really behind, according to him), 7 states work usually best as there are many to discriminate between, but also not too many to be able to see statistical significances between conditions.

Our study was the first one to apply this approach in animal models and in anesthetized. We tested this approach using either 5, 6 and 7 brain states. As you can see in the figure 5 dedicated at this part in our publication (Rahal et al., 2020 Sci Report), we obtained the same results, i.e. the same definition of states (for the 5 common) and the same statistical significance between our two experimental groups, suggesting that the approach is very robust.

Were you able to find physiological interpretations to the corresponding correlation matrices?

S. Pezet: In the discussion we elaborate on the neurobiological meaning of these states. I encourage you to read it. But in short: as the analysis in our study is performed on the phase of the signal,

- 1. The control animals spend most of their time in state 1, in which the signal of all ROI is on phase, which means that it is synchronous
- 2. In arthritic animals, they spend significantly less time in this state and more in two others, in which the synchrony in the somato-motor network is interrupted. We discuss in detail how one of these states/matrix is from a neurobiological point of view, due to the peripheral firing of nociceptors that occurs in the inflamed paw and its electrophysiological correlate in brain areas dedicated to the sensory component of this inflamed paw.

Is it possible to use fUS to assess drug permeability across the blood-brain barrier?

B. Vidal: If a drug produces CBV changes and it is not associated with changes in systemic parameters such as the blood pressure, it is an argument in favor of a crossing of the BBB, although not a straightforward demonstration. When this is possible, the drug should be compared with another drug that target the same receptors but does not cross the BBB).

Dr. Vidal mentioned there is a skull preparation before transcranial imaging of the brain. Is there any specific preparation to improve fUS coupling for the spinal cord imaging?

S. Pezet: Yes, we had to perform a laminectomy.

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Contact Information

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