Ultra-small voxel spectroscopy

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Spectroscopy of the mouse presents several challenges: The small size of the animal implies that the measurement location is typically close to the susceptibility interface between the diamagnetic mouse and paramagnetic oxygen in air and it implies small VOI on the order of µl to localize to functionally distinct regions, which represents a challenge for sensitivity.

For most localized spectroscopy applications contemporary shim coil designs permit elimination of much of the macroscopic susceptibility effects in mouse brain. These advances are likely to be of benefit to mouse imaging in general: For example, higher-order shimming has been shown beneficial for imaging sequences that are prone to such susceptibility effects, such as single-shot gradient echo EPI.

Sensitivity can be optimized: Using e.g. quadrature surface coils at least for reception allow to greatly improve sensitivity and thus reduce acquisition time compared to using volume coils as transceivers which incurs sensitivity losses, due to the small filling factor of the mouse brain.

Sensitivity has been shown to improve substantially when using high magnetic fields, combined with short echo times, allowing the measurement of the neurochemical profile in functionally distinct brain regions, as illustrated for mouse hypothalamus, shown in the Figure below:

Left: Neurochemical profile and its over 20 biomarkers accessible in rodent brain. Right: 1H NMR spectroscopy of 4µl volume of the hypothalamus at 14.1 Tesla compared to 3µl volume measured in the hippocampus using SPECIAL localization (TE=2.8ms). In both locations, more than 20 constituents of the neurochemical profile were quantified with a precision better than 30%. Note the comparatively low taurine and the high GABA content in the hypothalamus (arrows), both hallmarks of the neurochemical profile in rodent hypothalamus. Data was acquired using a 10mm quadrature surface coil as transceiver.
Clearly, a spatial resolution allowing the measurement of a comprehensive neurochemical profile is feasible in functional regions of the mouse brain: Examples to-date include, but are not limited to stroke, cancer models, and a plethora of transgenic models.

These approaches can be extended to μl spatial resolution using chemical shift imaging, which is a spatial resolution comparable to what is achievable with animal PET imaging.

**Summary:** The measurement of the neurochemical profile with microliter spatial resolution is routinely achieved in murine brain, allowing for a quantitative measurement of more than 20 biomarkers, covering membrane metabolism, energy metabolism, neurotransmitters, antioxidants and osmolytes (Figure 2). Such a highly quantitative, sensitive approach is likely to yield important insights into the function of many genes and mouse models of disease.

**Suggested reading:**

**Review articles**


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