

# Methodology of Magnetic Resonance Spectroscopy in Transgenic Mouse Models

(Methodology of proton MRS in mouse models)

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Proton magnetic resonance spectroscopy (MRS) provides a non-invasive way to quantify metabolites *in vivo* which can be of great interest for the studies of neurodegenerative disorders in which no biomarkers currently exist and for drug development studies in which biomarkers have been identified. Usually, drug development studies require sacrificing large numbers of mice in order to histologically assess therapeutic efficacy. *In vivo* MRS assessment of drug effect could in theory greatly reduce the numbers of mice needed for such studies thus accelerating drug development.

Eighteen metabolites can be measured and quantified separately in the brain of rodents at ultra high magnetic field strengths (1-3). Each observable metabolite can potentially provide unique information about the degenerative processes, because metabolites levels are sensitive to different *in vivo* pathological processes at the molecular or cellular levels. However, to observe small changes related to the progression of the disease or therapeutic efficacy of the drugs, *in vivo* MRS data need to be acquired from many mice and to have high reproducibility. It is very important to obtain the same quality of the data every time from the same brain region.

The following topics will be covered in this presentation:

- design of the mouse holder (4)

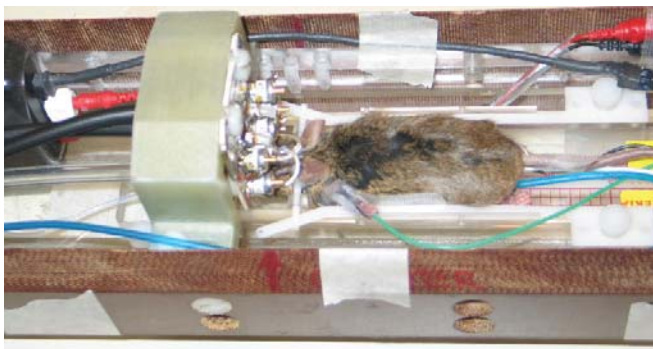


Figure 1. Coil and mouse holder. View from above with all the monitoring equipment connected – mouse head is held in place with adjustable plastic side clamps and an adjustable incisor bar. The nose is inserted into a cone which supplies anesthesia.

- protocols
- voxel positioning
- B<sub>0</sub> shimming
  - hardware requirements
  - automatic methods – FAST(EST)MAP (5,6)
- optimization

- calibration of RF pulses to check the performance of the system and the coil
- water suppression
- pulse sequences
  - PRESS (7)
  - ultra short echo-time sequences: STEAM (8) and SPECIAL (9)
  - LASER (10)
- data acquisition
  - single scans to perform both frequency and phase correction
  - reference water scan to perform eddy current correction
- data analysis
  - LCModel (11) or MRUI (12)
    - measured or simulated basis sets
    - experimental macromolecule spectrum (1)

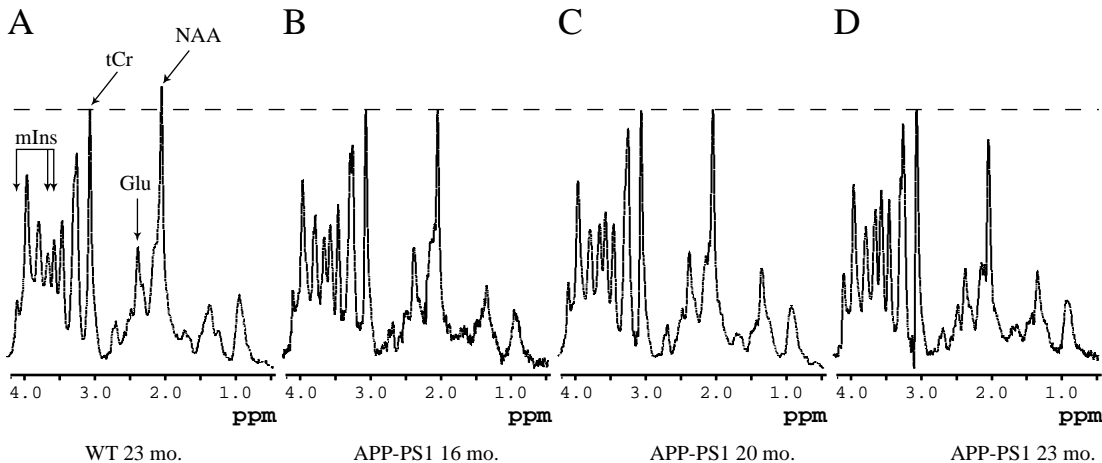


Figure 2. The detection of changes in the brain of the concentration of N-acetylaspartate, glutamate, and *myo*-inositol in transgenic mouse model of Alzheimer's disease (B-D) as compared to wild-type (WT) mouse (A) (13). Localized *in vivo*  $^1\text{H}$  MRS spectra obtained at 9.4 T from 18  $\mu\text{L}$  voxel placed in the cortex and hippocampus with LASER sequence at  $T_E = 28$  ms.

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