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Review

The neurochemical profile quantified by *in vivo* ^{1}H NMR spectroscopy

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ABSTRACT

Proton NMR spectroscopy is emerging from translational and preclinical neuroscience research as an important tool for evidence based diagnosis and therapy monitoring. It provides biomarkers that offer fingerprints of neurological disorders even in cases where a lesion is not yet observed in MR images. The collection of molecules used as cerebral biomarkers that are detectable by ^{1}H NMR spectroscopy define the so-called "neurochemical profile". The non-invasive quality of this technique makes it suitable not only for diagnostic purposes but also for therapy monitoring paralleling an eventual neuroprotection. The application of ^{1}H NMR spectroscopy in basic and translational neuroscience research is discussed here.

Contents

Abbreviations: AD, Alzheimer's disease; ALS, amyotrophic lateral sclerosis; BOLD, blood-oxygen-level dependence; CNS, central nervous system; CSI, chemical shift imaging; CRLB, Cramér-Rao lower bound; fMRI, functional MRI; GABA, γ-aminobutyrate; Glx, glutamate plus glutamine; GPC, glycerylphosphorylcholine; GSH, glutathione; HD, Huntington's disease; MRI, magnetic resonance imaging; MRS, magnetic resonance spectroscopy; NAA, *N*-acetylaspartate; NAAG, *N*-acetylaspartylglutamate; NMDA, *N*-methyl-D-aspartate; NMR, nuclear magnetic resonance; PCho, phosphorylcholine; PD, Parkinson's disease; PE, phosphorylethanolamine; PET, positron emission tomography; SCA1, spinocerebellar ataxia type 1; TCA, tricarboxylic acid; VOI, volume of interest; OVS, outer volume suppression; SAR, specific absorption rate; AFP, adiabatic-full-passage; AHP, adiabatic-half-passage; RF, radiofrequency; TE, echo time; TR, repetition time; SNR, signal-to-noise ratio; 3NP, 3-nitropropionic acid; BBB, blood-brain-barrier.

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Introduction

Enormous advances are occurring in the elucidation of the pathogenesis of neurological disorders. Their genetic characterization and the creation of transgenic mice developing human-like phenotypes of neuropathologies and neurodegeneration have greatly contributed in the effort for revealing the biochemical mechanisms of disease development and progression. We have now reached the moment when diagnostic tools are required to be reliable, applicable in a non-invasive way and to make a bridge between the clinical application and basic research. ^{1}H NMR spectroscopy is a potentially valuable, if not the best candidate to fulfill this role, since it allows monitoring brain neurochemistry in humans and animal models of neurological disorders in a non-invasive way, thus applicable longitudinally to monitor degeneration during disease progression or recession upon effective therapeutic intervention. Since exactly the same methodology can be applied to the human and to laboratory animals, it can be translated to the clinical routine. However, ^{1}H NMR spectroscopy of the rodent brain is technically challenging. These challenges of spectroscopy in rodents and particularly in mice had to be overcome to obtain reliable and quantifiable data. The small size of the animal's head implies that the region of interest for the NMR measurement is typically close to the interface between the diamagnetic tissue and the paramagnetic oxygen in air, thus inducing strong B_0 inhomogeneity. Efficient minimization of B_0 inhomogeneity (shimming) is required to achieve increased spectral resolution. Macroscopic susceptibility effects in different regions of the rodent brain can be eliminated with the use of contemporary shim coil designs for high order shimming. The inherently small size of the region of interest is further reduced when one aims to localize the spectra not only within the brain but to functionally different cerebral areas, thus reducing sensitivity that is the main intrinsic challenge of NMR spectroscopy. Sensitivity can, however, be optimized using for example quadrature surface coils for signal reception rather than using a transceiver

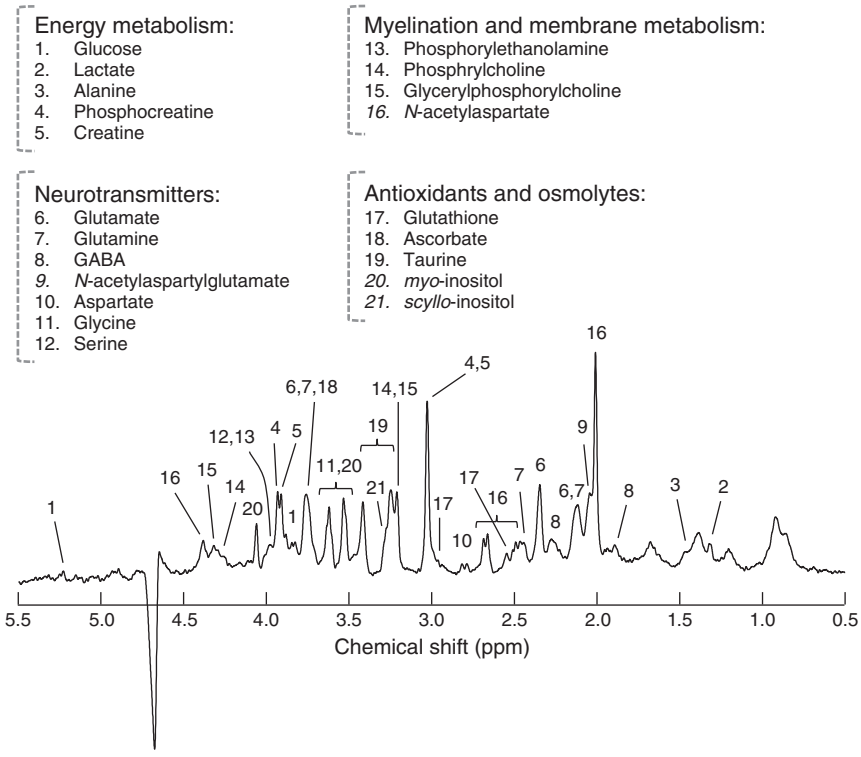

Fig. 1. Compounds detected in the brain with *in vivo* ^{1}H NMR spectroscopy. Spectrum was acquired from the rat hippocampus at 14.1 T using SPECIAL.