Research article

NMR IN BIOMEDICINE

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MR elastography in a murine stroke model reveals correlation of macroscopic viscoelastic properties of the brain with neuronal density

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The aim of this study was to investigate the influence of neuronal density on viscoelastic parameters of living brain tissue after ischemic infarction in the mouse using MR elastography (MRE). Transient middle cerebral artery occlusion (MCAO) in the left hemisphere was induced in 20 mice. *In vivo* 7-T MRE at a vibration frequency of 900 Hz was performed on days 3, 7, 14 and 28 ($n = 5$ per group) after MCAO, followed by the analysis of histological markers, such as neuron counts (NeuN). MCAO led to a significant reduction in the storage modulus in the left hemisphere relative to contralateral values ($p = 0.03$) without changes over time. A correlation between storage modulus and NeuN in both hemispheres was observed, with correlation coefficients of $R = 0.648$ ($p = 0.002$, left) and $R = 0.622$ ($p = 0.003$, right). The loss modulus was less sensitive to MCAO, but correlated with NeuN in the left hemisphere ($R = 0.764$, $p = 0.0001$). In agreement with the literature, these results suggest that the shear modulus in the brain is reduced after transient ischemic insult. Furthermore, our study provides evidence that the *in vivo* shear modulus of brain tissue correlates with neuronal density. In diagnostic applications, MRE may thus have diagnostic potential as a tool for image-based quantification of neurodegenerative processes. Copyright © 2013 John Wiley & Sons, Ltd.

Keywords: MR elastography; mouse brain; stroke; ischemia; middle cerebral artery occlusion; neuronal density; viscoelastic network

INTRODUCTION

The interruption of blood flow in a cerebral artery causes brain ischemia with a dramatic impact on brain metabolism and function. The pathogenesis of stroke and tissue repair after stroke involve multiple transient events and permanent reorganization processes, including vascular dilatation, neovascularization, inflammation, neuronal decline and gliosis (1–4). At autopsy, stroke areas are recognized as being softer than surrounding tissue or, conversely, present with higher stiffness when stroke repair with scar formation has occurred. As such, the viscoelastic properties of the brain provide biomarkers which are sensitive to the inherent mechanical constitution of cerebral parenchyma, and which change significantly in response to the disruption of cerebral blood flow and the following cascade of tissue degradation and regeneration processes (5,6).

In a recent study by Martín *et al*. (6), the tissue's mechanical response to an altered vessel size and vascularization after middle cerebral artery occlusion (MCAO) in rats was analyzed by ultrasound shear wave imaging (SWI) (7). The authors observed tissue softening in the hemisphere affected by stroke 1 day after the injury, suggesting the sensitivity of the brain's mechanical properties to the loss of structural organization by ischemic infarction. The authors of this study also observed bilateral angiogenesis in response to transient MCAO, whereas the decline in elasticity was measured by SWI only in the hemisphere containing the ischemic lesion.

An alternative method of elasticity imaging in small animal brains is MR elastography (MRE) (8–12). Recent studies have shown that demyelination and inflammation reduce the elasticity of brain

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Abbreviations used: *AD, Alzheimer's disease; ANOVA, analysis of variance; FLASH, fast low-angle shot; FOV, field of view; GFAP, glial fibrillary acidic protein; MCAO, middle cerebral artery occlusion; MRE, MR elastography; MS, multiple sclerosis; MSG, motion-sensitizing gradient; NeuN, neuron count; NPH, normal pressure hydrocephalus; ROI, region of interest; SWI, ultrasound shear wave imaging.*