The viscoelastic response of the human brain to functional activation detected by magnetic resonance elastography

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Target audience: Physicists, physicians and psychologists interested in the relationship between brain function and mechanical tissue properties.

Background: Mapping of brain function is an active area of research. Blood oxygenation level dependent (BOLD) functional MRI or NIRS are widely used for assessing regional brain activity based on the relationship between cerebral blood flow and neuronal activation (1). Other mechanisms such as ionic current flows, consumption of metabolites or micro morphological changes have been exploited for functional brain mapping by EEG, MEG, PET or functional DTI (2). Since both hemodynamics and micro architecture can influence the gross viscoelastic properties of the brain we hypothesize that cerebral MR elastography (MRE) is sensitive to brain activity (3).

Purpose: To study the sensitivity of viscoelastic properties of the brain to visual stimulation and to test the feasibility of functional MRE (fMRE).

Methods: fMRE experiments were performed in a total of 57 volunteers on a 3T MRI system equipped with a binocular visual stimulation system for the projection of an alternating black-white checkerboard (8 Hz) during the scan. Vibrations of 25, 30, 40 and 50 Hz were induced into the brain by a head cradle mounted to a nonmagnetic driver. Wave images were acquired by a single shot spin echo EPI sequence with motion encoding gradient of 1 cycle of 37 Hz and 35 mT/m amplitude. Two different sequence designs were realized in order to test time course and regional variation of the brain's mechanical response to visual stimulation. The first task (fast fMRE) was achieved by acquisition of 5 slices of two in-plane motion field encoding directions and 4 wave dynamics within 8 seconds synchronized to visual stimulation so that 10 full MRE data sets covered one of 6 on-off phases of stimulation. In the second experiment (3DfMRE) we acquired 7 contiguous slices, with 3 field components, 8 wave dynamics within 36 seconds synchronized to visual stimulation. Such set of data was acquired 10 times in order to capture 5 on- and 5 off stimulation phases. Fast fMRE was applied in 3 groups of 10 volunteers each with 4 vibration frequencies from 25 to 50 Hz including two reference fMRE experiments (no visual stimulation). 3DfMRE was applied to a group of 27 volunteers at 25 and 30 Hz vibration frequency. Data processing was based on direct inversion of the Helmholtz equation according to its magnitude representation as proposed in (4) yielding the magnitude shear modulus |G*|.

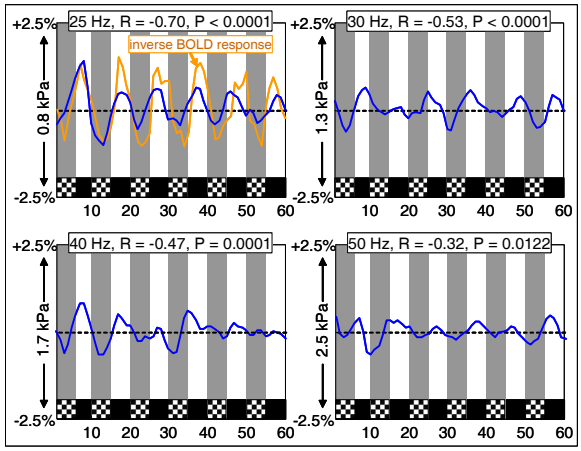

Fig.1: Fast fMRE at four mechanical excitation frequencies. The global response of |G*| to visual stimulation (averaged within 5 transversal slices) is shown over 60 repetitions. In addition to the 25-Hz response, the inverse BOLD effect is shown which was derived by standard 3D fMRI examined in the same subjects. Group size is N=10 by combining two frequencies in one group. In all experiments a decrease in |G*| is seen due to visual activation of the brain.

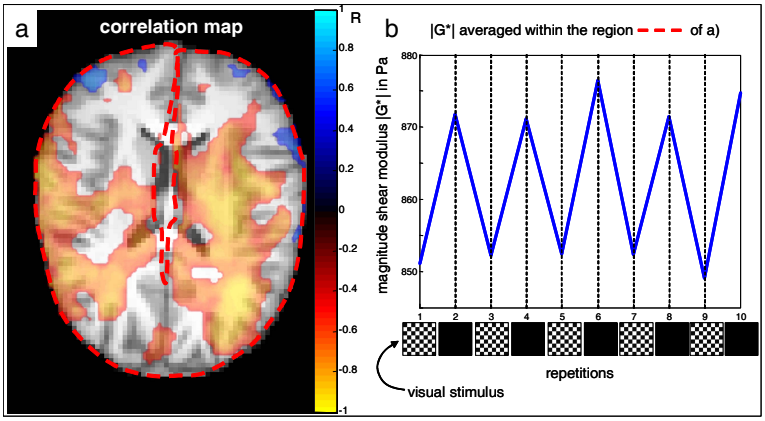

Fig.2: 3DfMRE analyzed after image registration in a group of 27 volunteers.

Results: Based on fast fMRE experiments, data in Fig.1 present a negative correlation coefficient R between |G*| and stimulus, i.e. decrease of |G*| due to activation. Furthermore, frequency resolved analysis reveals a decreasing |R| with increasing drive frequency indicating the involvement of poroelastic effects in fMRE since fluid- and vascular contributions to soft tissue's viscoelastic properties are expected to be higher at lower dynamics. Therefore, 3DfMRE for the study of regional effects was applied at low drive frequencies of 25 and 30 Hz. Fig.2 demonstrates the group-averaged distribution of R after image registration in a transversal brain slice angulated according to the calcarine sulcus to cover the visual cortex. A diffuse viscoelastic response to activity is seen not localized to the visual cortex.

Discussion: To our knowledge, this is the first study of the human brain's mechanical response to functional activation. We observed weak disseminated changes in the order of 2.5% of cerebral viscoelasticity by MRE with higher sensitivity at very low vibration frequencies of 25 and 30 Hz compared to 40 and 50 Hz. The repetition of fMRE using different drive frequencies and image acquisition protocols consistently showed decrease of brain viscoelasticity |G*| due to functional activation. In contrast to activity patterns revealed by BOLD fMRI, the viscoelastic response to brain function appears to be a global phenomenon which may be transmitted by the alteration of micro vascular pressure.

Conclusion: Our results provide first evidence of the sensitivity of cerebral MRE to brain function. Using fast single shot acquisition techniques synchronized to blocks of visual stimulation revealed a disseminated reduction of the brain's viscoelasticity modulus (magnitude of the shear modulus) due to activation. Further developments including volumetric strain MRE (5) and intrinsic mechanical stimulus MRE (6) could foster improved understanding of the fundamental physiological relationship between multiphasic tissue mechanics, hemodynamics and brain function.

References: (1) Ogawa et al. Proc Natl Acad Sci USA 1992;89:5951-5955. (2) Le Bihan et al. Proc Natl Acad Sci USA 2006;103:8263-8268. (3) Sack et al. Soft Matter 2013;9:5672-5680. (4) Hirsch et al. Magn Reson Med 2013;DOI 10.1002/mrm.24674. (5) Hirsch et al. Phys Med Biol 2013;58:5287-5299. (6) Weaver et al. Phys Med Biol 2012;57:7275-7287.