HIGH-RESOLUTION MAGNETIC RESONANCE IMAGING OF MECHANICAL PROPERTIES OF THE BRAIN

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EXECUTIVE SUMMARY

There is a large and growing body of evidence to support the interplay of mechanical properties of the human brain being affected by and affecting the function of the human brain. The ability to quantitatively assess the structural integrity of the brain using noninvasive techniques such as magnetic resonance imaging (MRI) may provide the necessary insight to understand the status and function of the living brain. Clinical MRI systems are capable of advanced quantitative imaging, both in high resolution and unique biomarkers, but they require significant technological development, tissue modeling, and computational resources. The Blue Waters environment has allowed for more rapid progress in all three areas through analysis of the computationally intensive inversion algorithms and validation of large experimental datasets. Two studies have been completed showing correlations between memory performance and hippocampal mechanical properties. Additionally, two ongoing studies look to characterize the structural–functional properties of the normal aging human brain.

RESEARCH CHALLENGE

The human brain changes throughout its lifetime, both in subtle and drastic ways. Subtle changes to the brain microstructure occur with lifestyle choices and normal aging. More drastic changes can come from traumatic injuries and neurodegenerative diseases. Quantitative MR imaging techniques provide the opportunity to interrogate the tissue microstructure for these changes, but traditional approaches require resolution on the order of the disruption of the microstructure, which is much smaller than the achievable spatial resolution of MRI. Magnetic resonance elastography (MRE) is a quantitative imaging method that is able to accurately estimate the viscoelastic material properties of the brain tissue, from the small grey matter regions (e.g., hippocampus) to large white matter (WM) regions. MRE relies on advanced imaging methods and a nonlinear inversion (NLI) to estimate the material properties. NLI is technically and computationally challenging but has shown it is sensitive enough to detect subtle changes in human brain structures during disease and even during exercise interventions in both healthy and diseased brains. Each brain requires the computationally expensive step of NLI, resulting in the need for significant resources for analysis of a single brain. Blue Waters enables running full studies of 10–50 subjects to answer specific questions about the relationship between brain material properties and function.

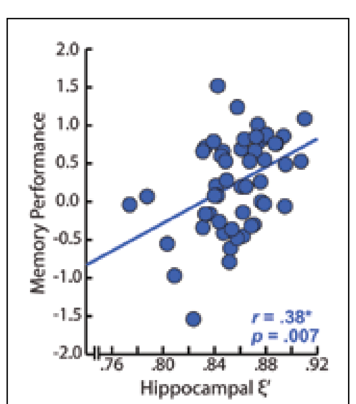

Figure 1: Hippocampal viscoelasticity is correlated with memory performance in young adults. This measure of hippocampal tissue health, unique to high-resolution MRE, provides a novel method to evaluate the brain, as illustrated by its improved sensitivity over hippocampal volume, a classical brain-health measure.

METHODS & CODES

MRE is a noninvasive quantitative technique for measuring the mechanical properties via the response of the tissue to externally applied shear waves. The full 3D mechanical waves are captured using synchronized motion-encoding imaging, then the material properties are estimated using an iterative, finite-element-based nonlinear inversion (NLI) of the heterogeneous, steady-state Navier equation [1–2]. The size of the computational problem initially required dividing the brain into smaller regions (called "subzones") for FEM meshing and optimization of properties at a local level, then reconstituting as a global solution. Blue Waters' combination of a large number of nodes, high-speed interconnect, and large memory systems enabled us to perform a parameter study of a wide range of subzone sizes to determine the dependence of the estimated mechanical properties on these parameters.

RESULTS & IMPACT

Four separate human studies were completed, or are underway, and focus on two areas of brain health: understanding the links between tissue mechanical properties and brain performance [3–4] and effects of normal aging on the microstructure of the human brain. We have built on previous findings with MRE in studies run at the Beckman Institute exploring the relationship between tissue viscoelasticity and memory to include an analysis of fitness effects, which are known to improve brain health. The positive relationship between hippocampal structure, aerobic fitness, and memory performance has been demonstrated at either end of the lifespan in children and older adults; evidence of this relationship among young adults, for whom the hippocampus is neither developing nor atrophying, is less consistent. Studies have typically relied on hippocampal volumetry (a gross proxy of tissue composition) to assess individual differences in hippocampal structure. Microstructural differences in hippocampal integrity may exist even among healthy young adults when volumetric differences are either absent or not diagnostic of tissue health or cognitive function.

In the current study, we investigated the relationship between hippocampal viscoelasticity from MRE and cardiovascular health, and their mutual effect on relational memory in a group of healthy young adults. We replicated our previous finding that hippocampal viscoelasticity correlates with relational memory performance. We extended this work by demonstrating better aerobic fitness, as measured by VO2max, was associated with hippocampal viscoelasticity that mediated the benefits of fitness on memory function. In contrast, hippocampal volume did not account for individual differences in memory. Therefore, these data suggest hippocampal viscoelasticity may provide a more sensitive measure of microstructural tissue organization and its consequences on brain performance among healthy young adults.

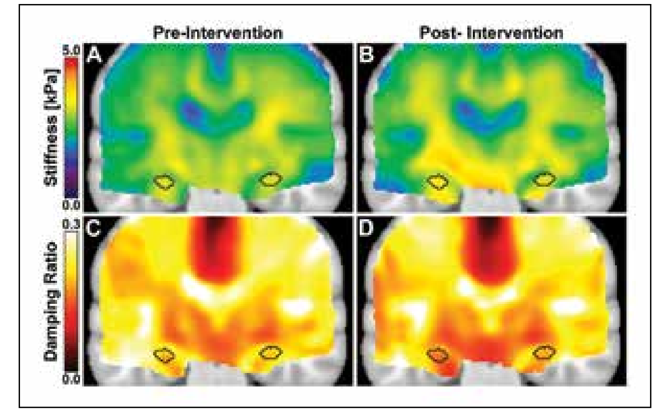

Figure 2: Hippocampal viscoelasticity is improved by exercise training in persons with multiple sclerosis. Exercise therapy improves brain health and cognition, and the MRE measure is used to evaluate the recovery of hippocampal integrity following intervention. It can be used to better design and deliver rehabilitative treatments in the future.

We followed up on the findings of relationships among hippocampal viscoelasticity, memory performance, and fitness by using MRE in a study of exercise training in persons with multiple sclerosis (MS). Five subjects with MS completed three-month exercise training, and we observed this intervention significantly improved their hippocampal viscoelasticity. Further, we observed the change in viscoelasticity correlated with the improvement in memory performance with training. These results highlight the sensitivity of the MRE measures of brain health as they relate to cognitive performance. By using a highly sensitive neuroimaging battery that includes MRE to monitor therapy, we can better understand the mechanisms contributing to brain health and recovery.

Finally, Blue Waters enabled a parameter study of NLI to further develop the NLI algorithms to improve the capabilities of quantitative imaging via a careful characterization of the effects of inversion parameters on the reconstructed material properties. Using the capabilities of Blue Waters' network and local memory, the size of the subzones was increased up to 15 times the previous subzone size, previously impossible on other systems. Additionally, processor speed afforded an investigation into increasing the number of conjugate gradient estimations at the subzone level to ensure proper convergence of the material property estimates. This study was the first of its kind in the breadth and depth of inversion parameter characterization.

WHY BLUE WATERS

The Blue Waters system provides a unique resource for MRI because it allows for rapid transfer of imaging data from the scanners and the low-latency memory transfers necessary for highly parallel computations. This is especially critical for quantitative, high-resolution MRI that inherently involves very large datasets and extensive computation. Blue Waters has enabled the refinement of these techniques and their translation in research by significantly reducing computational burden.

PUBLICATIONS AND DATA SETS

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Anderson, A.T., et al., Inversion Parameters based on Convergence and Error Metrics for Nonlinear Inversion MR Elastography. *25th Annual Meeting of the International Society for Magnetic Resonance in Medicine*, Honolulu, Hawaii, April 22–27, 2017.

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