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"Development of neuroimaging biomarkers of cerebrovascular integrity via multi-echo, multi-contrast functional MRI"

Abstract:

Alzheimer's disease (AD) may benefit from biomarkers that sensitively detect changes early in the disease course when therapeutic intervention is optimal. Vascular co-morbidities are common in AD, and neuroimaging methods such as cerebrovascular reactivity (CVR) may yield an ideal biomarker of vascular integrity. There are several technical challenges to measuring CVR in a clinical population that could limit the robustness of CVR as an imaging biomarker. Functional magnetic resonance imaging (fMRI) is commonly used but is most sensitive to large draining veins in the brain, whereas the pathological changes associated with AD and many vascular diseases are thought to be localized in the microvasculature. Moreover, there are a variety of different CVR paradigms used, some of which are not suitable for studies of clinical populations due to discomfort or dependence on patient compliance. To address these challenges, a combined spin- and gradient-echo (SAGE) fMRI method was developed, optimized, and validated for CVR estimation. SAGE-fMRI was shown to improve image quality compared to single-echo fMRI and provide two complementary analyses simultaneously on total and microvascular scales, the latter of which is more spatially specific to AD pathology. SAGE was further optimized by introducing a rapid fitting method for the multiple echoes, drastically reducing computational demand and improving feasibility of implementation. Moreover, SAGE-fMRI improved repeatability and reliability of CVR estimation compared to single-echo fMRI for multiple CVR paradigms. The optimized SAGE-fMRI CVR protocol was applied in the context of healthy aging (HC) and vascular pathologies including AD and vascular dementia (VaD). VaD CVR was the most reduced compared to HC, followed by AD. SAGE-fMRI CVR may be able to differentiate between cohorts with vascular pathologies and serve as an imaging biomarker of vascular integrity on total and microvascular scales, which could be relevant to the study of various cerebrovascular diseases.