Differential Effects of Age and Hypertension on Brain Anatomy and Physiology Assessed by Regional T2* Relaxometry and Volumetry

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Introduction: Brain aging is a dynamic process characterized by differential regional changes. Substantial individual variability is apparent in cognitive and brain aging trajectories; modifiers of the aging process are poorly understood. Vascular changes have been suggested as one of the major causes of age-related functional decline and it is possible that reduction in microvascular function underlies structural and functional changes observed over the lifespan. The purpose of this study was to first examine the effects of normal aging on a regional basal metabolic brain measure (T2*) and to further assess the association between regional brain volume and T2*. Secondly, we sought to determine to what extent the T2*-age associations are influenced by vascular risk factors (i.e., hypertension).

Materials and Methods: Participants (113 healthy adults, ages 19-83) were screened for history of cardiovascular, neurological or psychiatric conditions, head trauma, thyroid problems, diabetes, drug and alcohol abuse, depression and dementia. Each received a high resolution T1-weighted MPRAGE sequence and an eight-echo gradient recall susceptibility-weighted imaging sequence (SWI) on a 1.5T scanner. Regional brain volumes were computed from six traced regions of interest (ROIs). For the T2* signal intensity estimates, the short echo (i.e., magnitude) images were used to identify the anatomical boundaries of the ROIs, which were extracted from the T2* maps within each of those 6 structural ROIs. All ROIs were manually demarcated with high reliability, ICC(2) > .90. Systolic and diastolic blood pressure were measured in all participants using a mercury sphygmomanometer with a brachial cuff. Detailed health questionnaires, including hypertensive status, medication and years since diagnosis were administered.

Results: Age was negatively associated with T2*, but the strength of the associations differed across the examined brain regions (Fig. 1). Older adults had lower T2* in the age-sensitive cortical regions (frontal, medial-temporal) and in the neostriatum, but not in the primary visual cortex. Hypertension was associated with reduced T2* above and beyond the effects of age, indicating a role of vascular mechanisms in brain aging (see Fig. 2). Smaller hippocampal and neostriatal volumes were associated with lower T2* in those regions.

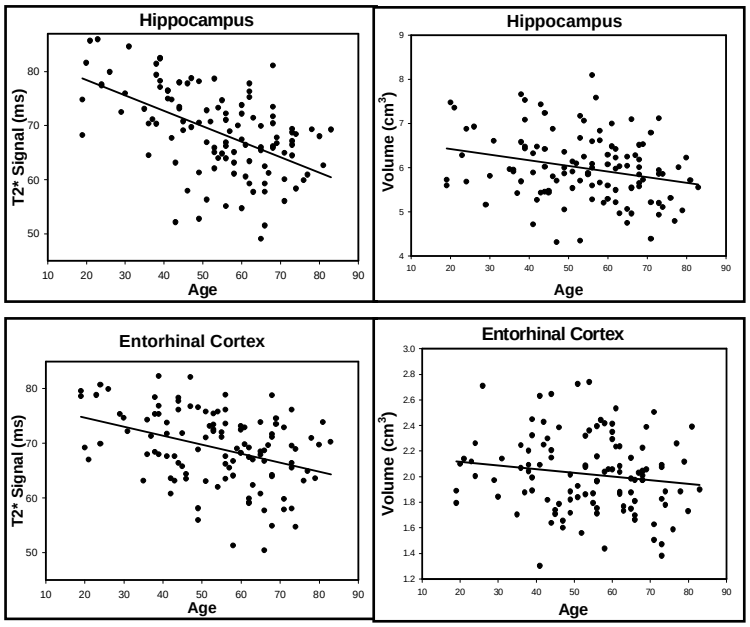

Figure 1: The age relation of T2* signal and brain volume in the hippocampus (top) and entorhinal cortex (lower). Age differences in T2* are stronger than those in brain volume.

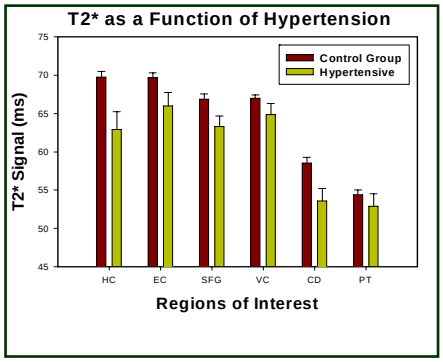

Figure 2. T2* signal in the hypertensive group is selectively reduced in age-sensitive brain regions compared to age, sex and education matched controls.

Conclusions: T2* is influenced by local iron content such as heme iron (deoxyhemoglobin) and non-heme iron (ferritin or hemosiderin). Thus, reductions in T2* may reflect age-related differences in the concentration of deoxyhemoglobin in veins, the presence of ferritin, which is known to accumulate with age most prominently in the basal ganglia and motor cortex, and/or the presence of hemosiderin from local microbleeds. Perhaps the most important finding in this work is that the age differences in T2* in the medial-temporal structures (HC and EC) were stronger than those seen in brain volume. Whether this is an expression of iron-related changes preceding local shrinkage can be resolved only in a longitudinal study.