Title: Association between structural changes in the brain and physical function in older women

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Background: Aging is associated with changes in brain integrity which has been connected with declines in physical function without signs of dementia. However, there is a gap in knowledge whether location and magnitude of integrity changes predict physical function status later in life. This study examined brain changes characterized by structural magnetic resonance imaging (MRI) associated with physical function in older women, a population vulnerable to physical disability.

Objectives: To determine the degree to which changes in brain volumes and ischemic lesions are associated with physical performance and muscle strength in older women

Methods: Repeat structural brain MRI scans were collected among 472 women enrolled in the Women's Health Initiative (WHI) study, aged 50-79 years old at randomization and without any prior stroke history. All participants were non-demented and scored highly on a test of global cognition (average modified mini-mental state exam score: 98+/-2 out of 100). Brain volumes and ischemic lesion volumes in the whole brain, white matter, gray matter, lobes, and basal ganglia regions were first scanned 8.0+/-0.6 yrs after randomization and obtained at a second scan 4.7+/-0.4 years later. Brain changes were adjusted for between-subject variation by dividing the difference score by the regional volume at the first MRI visit. The Short Physical Performance Battery (SPPB) containing balance, walking, and chair stand tests, along with hand grip strength were measured 2.5+/-0.5 yrs after the second MRI scan. Regression models adjusted for demographics, behavioral factors, medical conditions, depression, global cognitive scores, and years between the second MRI visit and physical function assessment were used to estimate the association between brain changes and functional outcomes.

Results: The analytic sample had a -0.5+/-0.4% decrease/year in total brain volume while experiencing a 0.1+/-0.4% increase/year of ischemic lesions across the entire brain. In unadjusted models, gray matter was observed to have the highest decrease in volume (-0.8±0.4%/year) whereas the basal ganglia region showed the highest increase in ischemic lesions (0.5+/-0.6%/year). Decreases in gray matter volumes and increases in white matter were negatively associated with grip strength ($p<0.05$, respectively) in fully adjusted models. Ischemic lesion increases in total brain, gray matter, frontal lobe, and parietal lobe were negatively associated with SPPB while increases in total brain, gray matter, frontal lobe, and occipital lobe were associated with grip strength ($p<0.05$ for all).

Discussion: These results indicate changes in white/gray matter volumes and losses in brain integrity (i.e. increased ischemic loads) in non-demented, cognitive healthy older women were associated with lower physical performance and muscle strength.

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