Brain Health and Frailty: Where Do We Go Next?

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Frailty is a multidimensional condition that makes older adults more vulnerable to adverse health events such as disability, hospitalizations and death (1, 2). The multidimensional (1) aspect of frailty makes it difficult to pinpoint its origins, but somehow cross-sectional studies have found that brain health is more deteriorated in frail individuals (3, 4). Research is now focused in finding biomarkers that are related to adverse events in older adults (5), thus raising the importance that brain health biomarkers, such as amyloid load and white matter lesions, could be associated with frailty severity.

Up to now, only cross-sectional studies have found that different markers of cerebral damage were found to be associated with frailty: 1) frail individuals were found to have higher amyloid load compared to non-frail individuals (4) and 2) frail older adults had more white matter lesions (3). Accordingly, two studies that used ancillary data from the Multidomain Alzheimer's Preventive Trial (MAPT) (6) study have found interesting results regarding the prospective associations between brain health and frailty. The first study which used the magnetic resonance imaging (MRI) data for the detection of white matter lesion has found that older adults with higher white matter lesions had a 6% likelihood of increasing their frailty phenotype score by 1 point after 3 years (7). White matter lesions can affect motor function and gait speed, thus increasing frailty severity risks.

In line with this, another study using positron emission tomography (PET) scans for the acquisition of brain amyloid load have found prospective and positive associations with a 19-item frailty index that used only items that were not directly linked to cognition. More specifically, this study found that brain regions, such as the putamen regions (anterior and posterior) and the precuneus regions were all associated with increased frailty after 3 years (8).

Higher amyloid load in specific regions such as the putamen and the precuneus play a role in coordination and motor function (9, 10). Finally, these studies point to the fact that the development of frailty can be promoted if the speed of accumulation of amyloid load and white matter lesions is accelerating. As such, during this stage, prevention strategies should be implemented to prevent the precocious appearance of frailty and maintain dependence in this population. Interestingly, a recent study from Buchman and colleagues (11) have shown that high levels of physical activity is associated with better function and cognition, independently of other brain pathologies. Thus, slowing down frailty could slow down Alzheimer's Disease (AD) pathology.

These studies add to the body of literature that frailty and AD pathology are both tightly associated and that one condition probably does not go without the other (12). In line with this, a recent and interesting study from Wallace et al (13) found that frailty status can modify the association with Alzheimer's Disease, increasing the potential influence of frailty in cognitive disorders. Finally, the recent contributions from our group (7, 8) and others (11, 13) are important contributions in this field, but future studies are needed to try and tease out the direction of the association between brain health and frailty. An observational study using a longer follow-up with many time-point measurements of brain imaging could be of importance by improving the precision of the trajectory for both outcomes.

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