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Stress over the lifetime has been shown to negatively impact brain structure and cognition in animal models. In addition, advancing age has been observed to have negative effects on brain structure and function. Lifetime stress may contribute to the observed detrimental effects of aging. One activity that has been shown to be beneficial for brain structure and cognition is aerobic exercise. Thus, the primary goals of the current study were to assess the effects of lifetime stress in older adult humans and to examine possible moderation of the effects of stress on brain structure and function in older adults through exercise engagement. Participants were 60 healthy older adults aged 55 to 87. MRI-based volumes of the prefrontal cortex, orbitofrontal cortex, hippocampus, and amygdala were obtained. Cognitive function was measured through a battery of cognitive tasks measuring immediate memory, working memory, executive functions, and processing speed. Data were also obtained through retrospective questionnaires on lifetime stress and exercise engagement. Smaller brain volumes associated with stress were demonstrated for the orbitofrontal cortex, amygdala. Lower capacity for cognitive functions of executive functions and processing speed with a nonsignificant trend for the hippocampus were also demonstrated. In addition, there was a non-significant trend for participants with higher levels of lifetime stress to demonstrate steeper age-related decline in immediate memory. There were non-significant trends for exercise engagement to moderate the effects of stress on orbitofrontal cortex and immediate memory: for individuals with lower amounts of stress, those who exercised more evidenced less age effects. The potential impact of exercise in moderating the impacts of stress on brain structure and function clearly warrant further research as well as exploration of such factors as amount of exercise, a threshold for beneficial exercise effects, and personality factors.