(P=0.021). Pearson's correlations examined the relationship between balance and mobility before surgery and change score after surgery. Patients with lower baseline DGI and MiniBest scores demonstrated the most improvement on follow-up testing (r=-0.70, p=0.001, and r=-0.59, p=0.006, respectively). In conclusion, revascularization of a carotid artery stenosis improves balance and mobility; the greatest improvements are observed in those patients that are the most impaired.

COGNITIVELY IMPAIRED OLD MICE DISPLAY CORRELATED REDUCTION IN CORTICAL NMDA RECEPTOR AND COMPLEX IV

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Cognitive decline in older adults represents a major challenge since cognitive impairment is found in 10% of those ≥ 65 and 50% ≥ 85. Thus it is increasingly important to understand the impact of aging on cognitive health. We performed a battery of tests to assess cognition in 6 month-old (n=12) and 24 month-old (n=8) C57BL/6J mice, equivalent to 30 and 70 year old humans, respectively, and also assessed protein markers in cortex for mitochondrial health and cognition. We found that aged mice displayed fewer spontaneous alternations in the T maze test (p=0.034) and lower recognition of novel objects (p=0.022). In addition, aged mice showed prolonged escape time in the Barnes maze (p=0.035), all of which taken together suggest reduced capacity for learning and recall. Aged mice also exhibited diminished nest building (p<0.001), revealing an impaired functional capacity analogous to the instrumental activities of daily living (IADL) geriatric assessment. We found reduced mitochondrial complex IV expression in the cortices of aged mice concomitant with less expression of N-Methyl D-Aspartate (NMDA) receptor subunits 1, 2A and 2B. The cortices from old mice also exhibited greater expression of immature brain derived neurotrophic factor (pro-BDNF). The alterations in NMDA receptors and pro BDNF are consistent with memory impairment and greater neuronal cell death. Therefore, aged mice exhibit significantly reduced recall and learning ability alongside marked alterations in mitochondrial complex, NMDA receptor, and pro-BDNF expression. Studies are underway to assess whether these molecular changes are responsible for the cognitive declines with aging.

CO-OCCURRENCE OF PHYSICAL AND COGNITIVE DECLINE IN VERVET MONKEYS (CHLOROCEBUS AETHIOPS SABAEUS)

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Age-related neurodegeneration associated with Alzheimer's (AD) disease begins in middle age, well before the onset of symptoms. Therefore, translational models to identify modifiable risk factors in middle-age are needed to understand etiology and identify therapeutic targets. Vervet monkeys (Chlorocebus aethiops sabaeus), like humans, naturally develop several risk factors for AD with age, including obesity, prediabetes, and hypertension. Furthermore, older vervets exhibit accumulation of amyloid and tauopathies, decreased brain volumes, and physical declines in gait speed, suggesting that these NHPs may be useful models of early AD-like neuropathology. Currently, we are investigating the extent to which cognitive and physical decline co-occur in 20 elder (mean age=23 years, ~equivalent to a human age of 80 years) and 10 middle-aged (mean age=11 years) females through assessments of physical performance, executive function, social cognition, and short-term memory. These measures are part of a larger study to integrate physical, social, and cognitive function with measures of body composition, metabolic profiles, CSF, blood, neuroimages, and neuropathology. While tests of social cognition and short-term memory are ongoing, assessments of executive function indicate that performance declines with age (N=26; p<0.05; R-squared=0.23). Furthermore, animals that exhibit slower gait speed also perform poorly on the executive function task (N=26, p<0.05; R-squared=0.25). These preliminary results suggest that accelerated aging co-occurs in multiple systems in vervets. This study will enable examination of temporal relationships between physical and cognitive declines. Ultimately, this comprehensive, integrative whole-body approach will help clarify the mechanisms underlying divergent aging trajectories and inspire interventions that promote multi-system healthy aging.

DETERMINING THE ROLE OF APOE4 IN AGE-RELATED CEREBROVASCULAR DECLINE

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Cerebrovascular decline occurs during aging and may be critical during prodromal phases of Alzheimer's disease (AD). The E4 allele of apolipoprotein E (APOE4) is the greatest genetic risk factor for AD and decreased longevity and studies suggest APOE4 increases risk for age-dependent cerebrovascular damage. To study the relationship between APOE4 and age-related cerebrovascular decline, male and female C57BL/6J (B6) mice carrying combinations of APOE alleles including APOE4 (risk) and APOE3 (neutral), as well as B6 controls were assessed at a variety of ages from 4 to 24 mos for cognitive ability, biometrics and cerebrovascular health including i) PET/MRI using 64Cu-PTSM (perfusion) and 18F-FDG (metabolism), ii) transcriptional profiling and iii) immunofluorescence. Despite no cognitive decline, male APOE4 mice showed hypo-perfusion and hypo-metabolism by 12 mos, while female APOE4 mice showed an uncoupled hyper-perfusion and hypo-metabolism phenotype. Transcriptional profiling showed differential expression of genes involved in regulation of cerebral perfusion, glucose transportation and metabolism in APOE4 mice. An age-dependent blood brain barrier compromise was also apparent in the brains of female APOE4 mice. Physical activity reduces risk for human AD and our data shows exercise