(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 impairments 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 sabaueus), 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...
improves cerebrovascular health in mice. However, the effects to cerebrovascular health in individuals carrying genetic risk factors such as APOE4 are not known. To determine whether exercise can overcome APOE4-dependent cerebrovascular damage, APOE mice are being exercised from 2-4 and to 2-12 mos. Transcriptional profiling and immunofluorescence will determine whether the benefits of exercise to the cerebrovasculature are modulated by genetic risk factors such as APOE4.

DOES INFLAMMATION MEDIATE THE ASSOCIATION BETWEEN SLEEP DURATION AND INCIDENT DEMENTIA AMONG OLDER ADULTS?

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Sleep duration is a risk factor for multiple health outcomes. Growing attention has been directed to the association between sleep duration and dementia; however, results were inconsistent and the mechanisms remained largely unknown. We hypothesized that elevated levels of inflammation markers—C reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α)—would mediate the association between sleep duration and dementia among older adults. Data were from the Health, Aging, and Body Composition Study; 3,010 participants free of dementia at baseline were included. Sleep duration was classified into: short (<6 hours), normal (6-8 hours), and long (>8 hours). Incident dementia was defined as (i) use of prescribed dementia medications, (ii) adjudicated dementia diagnosis, or (iii) a race-stratified cognitive decline >1.5 SDs from the baseline mean. We used Cox models to examine the associations among sleep duration, inflammation, and dementia. The average age was 73.6 years (SD=2.9); 49% were male and 41% were black. During 10 years of follow-up, 515 participants (17.1%) developed dementia. Long sleep duration was associated with higher hazard of dementia than normal sleep duration (HR=1.50, 95%CI=1.02-2.21). The association was attenuated by approximately 10% when CRP or IL-6 was added in the model. When all three inflammation markers were included in the model, the hazard ratio of long sleep duration was reduced by nearly 30% and no longer significant (HR=1.36, 95%CI=0.89-2.08). Long sleep duration was associated with high risk of incident dementia among older adults and the association was partly explained by elevated levels of inflammation markers.

EFFECT OF OSTEOARTHRITIS ON PREFRONTAL CORTICAL ACTIVATION PATTERNS DURING DOWNWARD REACHING IN OLDER WOMEN

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Downward reaching may lead to falls in older adults, but the underlying mechanisms are poorly understood, particularly in older women with osteoarthritis. Given the importance of attentional resources when maintaining balance in balance-demanding conditions, functional near-infrared spectroscopy may provide a lens to the attentional resource allocation needed to maintain balance while reaching down to the ground with or without full contact with the floor. We examined the changes in the executive control of downward reaching movements in older women with osteoarthritis. We hypothesized that prefrontal cortical activation would be higher in older women with osteoarthritis, compared to age-matched controls, particularly as the balance demands increased. Older women with osteoarthritis (n=7, mean±SD age: 66±3 years) and age-matched controls (n=10, mean±SD age: 67±6 years) were recruited from the local community. The effect of the base of support and target position (toe or maximal forward distance along ground) on attentional resources in older women with osteoarthritis were evaluated using the average oxygenated hemoglobin levels as a measure of prefrontal cortical (PFC) activation. Significant base of support by cohort and target by cohort interactions were observed on average PFC activation levels (P<0.005). As expected, PFC activation levels increased as the contact with the floor decreased and as the target distance increased, but older women with osteoarthritis were unable to increase their PFC activation levels as much as age-matched controls. In conclusion, these data suggest that older women with osteoarthritis may not be adequately modulating attentional resources to meet high-balance demanding tasks.

EFFECTS OF CNS DEMYELINATION AND MYELIN RECOVERY ON URINARY PHYSIOLOGY

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Multiple sclerosis (MS) is a chronic inflammatory demyelinating disease of the central nervous system (CNS). Of note, over 80% of MS patients have urinary symptoms as one of their earliest symptoms. Since MS patients often live into older age, urinary incontinence and retention are significant problems for which few if any effective preventive or therapeutic options are available. The mechanisms by which MS contributes to urinary dysfunction are not well understood. We propose to elucidate the impact of demyelination on urinary performance using the cuprizone model, a model used to study the effects of CNS demyelination and spontaneous remyelination. We hypothesize that CNS demyelination in the cuprizone model will result in aberrant changes in urinary function, and that after remyelination occurs this dysfunction will be alleviated. C57Bl/6 mice were treated with cuprizone (0.2% w/w) for four weeks to induce demyelination. One group was allowed four additional weeks to recover from demyelination, while the other continued cuprizone treatment. Following this eight-week treatment, pressure/flow cystometry, electromyography, and molecular studies were performed to assess demyelination-induced differences in urinary performance. Cuprizone-recovery mice displayed improvements in cystometric function compared to their demyelinated littermates, as seen through improved volume sensitivity and voiding efficiency. Pharmacologic studies showed no significant changes in contractile responsiveness. Thus, we conclude that CNS demyelination results in aging-like phenotype and urinary dysfunction consistent with that observed in clinical disease. Therapeutics aimed at increasing the remyelination potential of the CNS neurons offer the possibility of alleviating urinary dysfunction associated with MS.