AGING EFFECTS OF MOTOR PREDICTION ON PROTECTIVE BALANCE AND STARTLE RESPONSES TO SUDDEN DROP PERTURBATIONS.

O. Sanders¹, H. Hsiao², D. Savin³, R. Creath¹, M. Rogers¹, 1. *University of Maryland School of Medicine*, 2. *Department of Kinesiology and Health Education*, 3. *University of Maryland, School of Medicine*

This study investigated the modulatory effects of self-triggered drop perturbations (SLF) on reducing startle-like first trial response (FTR) magnitude evoked by externally-triggered (EXT) drop perturbations in younger and older adults. Ten healthy older (71.4 ± 1.44 years) and younger adults (26.2 ± 1.63 years) stood atop a moveable platform and received blocks of twelve consecutive EXT and SLF drop perturbations. Following the last SLF trial, participants received an additional EXT trial spaced 20 minutes apart to assess retention (EXT RTN) of any modulation effects. Electromyographic (EMG) activity was recorded bilaterally over the sternocleidomastoid (SCM), vastus lateralis (VL), biceps femoris (BF), medial gastrocnemius (MG), and tibialis anterior (TA). Whole-body kinematics and kinetic data were recorded with motion analysis. Stability in the antero-posterior direction was quantified using the margin of stability (MoS). Younger and older adults showed reduced SCM peak amplitude responses during SLF and EXT RTN trials. VL/BF and TA/MG coactivation were reduced during SLF FTR compared to EXT FTR ($p < 0.05$) with reduced peak vGRFs both younger and older adults ($p < 0.05$). Older adults increased their MoS during SLF FTR compared to EXT FTR ($p < 0.05$). Both groups performed more eccentric work during SLF trials compared to EXT ($p < 0.05$). These findings indicated that abnormal startle effects with aging may interfere with balance recovery and increase risk of injury with external balance perturbations. Motor prediction may be used to acutely mitigate abnormal startle/postural responses with aging.

AGING EFFECTS ON BRAIN METABOLISM AND ITS RESPONSE TO MENTAL ACTIVITY

A. Vlassenko, L. Couture, T. Durbin, M. Raichle, M. Goyal, *Washington University School of Medicine*

In young adults, task performance and sensory stimulation induces an increase in total glucose metabolism (CMRGlc) and cerebral blood flow (CBF) but only slight change in oxygen metabolism (CMRO2) in the stimulated brain region. Aging is associated with specific topographic changes in the resting state brain metabolism, especially in aerobic glycolysis (AG), which decreases across the lifespan. AG has a role in multiple metabolic pathways associated with neuroprotection, biosynthesis, synaptic plasticity and learning. In this study, we evaluated effects of aging on changes in AG, CMRGlc, CMRO2 and CBF in response to mental activity. Positron emission tomography (PET) studies using inhalation of ^{15}O -CO and ^{15}O -O₂, and injection of ^{15}O -water, and ^{18}F -fluorodeoxyglucose (FDG) were performed in 29 healthy cognitively normal participants (10 young and 19 older adults) at rest and during performance of the word stem completion task. AG, CMRGlc, CMRO2 and CBF were calculated for brain regions defined using FreeSurfer software and partial volume correction. Topographic analysis of this PET imaging data demonstrated that in young adults, the task condition evoked both increases (visual cortex) and

decreases (anterior cingulate, precuneus) in AG, CBF and CMRGlc, whereas minimal changes were seen in CMRO2. These findings were not significantly different in the older participants compared to the younger adults. The dissociation between aging related differences in resting brain AG and their absence in task-induced AG suggest that the drivers of resting brain AG might differ from those causing a rise in AG during brain stimulation.

AGING-ASSOCIATED LOSS OF ARNT SIGNALING IMPAIRS SKELETAL MUSCLE REGENERATION

B. Li¹, I. Sinha², D. Sakthivel¹, K. Udeh¹, A. Panayi³, T. Kah Yong⁴, S. Bhasin⁵, A. Wagers¹, 1. *Ms.*, 2. *Division of Plastic Surgery, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts*, 3. *Brigham and Women*, 4. *Mr*, 5. *Brigham and Women's Hospital*

Purpose: Skeletal muscle regeneration is required for the maintenance of muscle mass in aging. Hypoxia signaling, including aryl hydrocarbon nuclear translocator (ARNT), is necessary to maintain regenerative potential. The present study evaluates whether loss of hypoxia signaling in aging directly limits skeletal muscle precursor (SMP) regenerative potential.

Methods: Young (Y, 8–12 weeks) and old (O, 21–23 months) mice were utilized to determine changes in regenerative potential and skeletal muscle hypoxia signaling that occur with aging. Whole muscle was utilized for immunoblotting, PCR, and fluorescence activated cell sorting for SMP isolation. HSA-Cre ER ARNTfl/fl mice were used to create mice with muscle specific loss of ARNT following activation.

Results: SMP frequency and myogenic potential decrease dramatically in aging ($p < 0.001$). Cross-sectional area in regenerating fibers decreases by 40% in O mice as compared to Y following injury ($p < 0.01$). In whole, hind-limb skeletal muscle, we found that ARNT levels are 4.7-fold lower by PCR ($p < 0.01$) and 5-fold lower by immunoblotting in O versus Y mice ($p < 0.01$). Young, tamoxifen-activated HSA-Cre ER ARNTfl/fl mice, created to mimic the loss of hypoxia signaling in old mice, exhibit an 80% skeletal muscle specific decrease in ARNT and VEGF expression and protein levels following injury ($p < 0.01$) and a 25% decrease in skeletal muscle fiber cross sectional area ($p < 0.01$) as compared to littermate controls.

Conclusion: Hypoxia signaling declines with aging and contributes to loss of skeletal muscle regeneration. Restoring the hypoxia pathway may promote regeneration and prevent muscle loss in aging.

AN INTEGRATED OMICS APPROACH FOR THE STUDY OF MILD AND SEVERE ALZHEIMER'S DISEASE IN POST-MORTEM HUMAN BRAIN

S. Graham¹, A. Yilmaz¹, X. An², S. Vishweswaraiah¹, U. Radhakrishna³, R. Bahado-Singh¹, B. Green⁴, M. Maddens¹, 1. *Beaumont Hospital-Royal Oak*, 2. *Queen's University, Belfast*, 3. *Beaumont Hospital-Royal Oak*, 4. *Queen's University, Belfast, United Kingdom*

Background: Alzheimer's disease is 6th leading cause of death in the United States and its prevalence is continuing to grow with our ever-aging population. Currently the etiology and pathophysiology of the disease is not fully