



## Mid Atlantic Regional Chapter of the American College of Sports Medicine

45<sup>th</sup> Annual Scientific Meeting, November 4<sup>th</sup>- 5<sup>th</sup>, 2022  
Conference Proceedings

International Journal of Exercise Science, Issue 9, Volume 11



### Maximal Fat Oxidation is Diminished in Individuals with Mild Cognitive Impairment

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Alzheimer's Disease (AD) affects approximately 6.5 million older adults and is currently the 7th leading cause of death in the United States. With cases of AD projected to triple within the coming decades as the population continues to age, great emphasis has recently been placed on developing methods to identify those at a higher risk of AD development at a possible early stage of the disease known as mild cognitive impairment (MCI). Mitochondrial dysfunction is one risk factor that may be useful in risk stratification. Metabolic flexibility represents the capacity of the mitochondria to oxidize a variety of fuel substrates (i.e., carbohydrates and fatty acids), and could assess mitochondrial health prior to the development of further risk factors. **PURPOSE:** To determine whether individuals with MCI display diminished metabolic flexibility in response to a graded exercise test. **METHODS:** 22 older adults with MCI and 21 sedentary healthy controls (HCs) matched for both age and sex underwent a Bruce Protocol on a treadmill to assess VO<sub>2</sub>max. Fat oxidation (FatOx) and carbohydrate oxidation (CHOOx) were calculated based on ventilatory equivalents using the equations FatOx = 1.67VO<sub>2</sub> - 1.70VCO<sub>2</sub> [L/min] and CHOOx = 4.585VO<sub>2</sub> - 3.2255VCO<sub>2</sub> [L/min], respectively. Unpaired t-tests were conducted to determine whether baseline or maximal FatOx and CHOOx were different between groups. **RESULTS:** The MCI and the HC groups were similar in age (73.5 ± 8.81 vs. 71.2 ± 6.33, p=0.33) and BMI (26.2 ± 4.92 vs. 26.8 ± 5.16, p=0.70). Baseline FatOx (0.09 ± 0.03 vs. 0.10 ± 0.05 g/min, p=0.47) and CHOOx (0.51 ± 0.17 vs. 0.59 ± 0.21 g/min, p=0.23) were not different between the MCI and HC groups. However, the HC group displayed a higher VO<sub>2</sub>max (1.32 ± 0.33 vs. 1.61 ± 0.47 L/min, p=0.027\*), greater maximal FatOx (0.31 ± 0.13 vs. 0.39 ± 0.10 g/min, p=0.018\*), and greater maximal CHOOx (1.89 ± 0.41 vs. 2.18 ± 0.49 g/min, p=0.047\*) than the MCI group. **CONCLUSION:** These findings suggest that maximal FatOx, CHOOx, and oxygen consumption are diminished in older adults with MCI and may reflect impaired whole body mitochondrial capacity and metabolic flexibility.