

older adults free of neuropathologies and clinically overt conditions. This symposium will first present clinical and epidemiologic justifications for operationalizing energy as a separate construct from fatigue and then will provide evidence on the underlying neurobiological correlates. Taken together, our results suggest perceived energy: a) overlaps with but is distinct from lower fatigability (Katz); b) may signal resilience against age-related declining mood and gait speed despite self-reported tiredness (Ehrenkranz); c) appear negatively influenced by Alzheimer's neuropathology (Dougherty); and d) may reflect a distinct spatial distribution of brain functional connectivity (Hengenius). Thus, this symposium will explore energy as a mechanism related to yet distinct from fatigue and its implications for both healthy aging and neuropathological processes.

#### ENERGY AND FATIGUE PREDICT GAIT SPEED AND MOOD DECLINE: RESULTS FROM THE HEALTH, AGING AND BODY COMPOSITION STUDY

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Older adults may report high energy alongside tiredness or vice versa; little is known about whether discordant self-reported energy (SEL) and tiredness predict trajectories of mood, cognition, or gait speed. SEL (0-10 scale dichotomized at median) and tiredness (present/absent) were obtained in 2,613 older adults (aged 74.6±2.87 years) and used to create four groups (energized/not tired, low energy/tired, energized/tired, low energy/not tired). Center for Epidemiologic Studies Depression Scale (CES-D) and gait speed were measured over 10 years; mixed effect models compared trajectories in these domains across each group with low energy/tired group as referent. Each group was significantly associated with CES-D and gait. Adjusting for demographics, the high SEL/not tired group showed the least decline in mood ( $\beta = -0.17$ ,  $p < 0.01$ ); the high SEL/tired group showed the least decline in rapid gait ( $\beta = 0.008$ ,  $p = 0.02$ ). High SEL may indicate resilience for mood and gait speed decline.

#### ENERGY AND EXHAUSTION MAY EXPLAIN DIFFERENT SUBDOMAINS OF PERCEIVED FATIGABILITY

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Fatigability is a more sensitive measure of one's perception of fatigue. To identify an appropriate fatigue question when a fatigability measure is unavailable, we examined associations between widely used global fatigue questions and perceived physical and mental fatigability. Participants (N=896, age=74.7±6.6, 58.1% women) from two aging

research registries completed the valid Pittsburgh Fatigability Scale (PFS, 0-50) and five global fatigue questions: energy level (0-10), running out of energy (0-5), feeling energetic (0-6), feeling tired (0-6), and feeling exhausted (0-6) over past four weeks. All fatigue measures were correlated ( $p < 0.0001$ ) with physical ( $|r|$  range=0.48-0.57) and mental fatigability ( $|r|$  range=0.31-0.39). "Energy level" and "feeling exhausted" had strongest associations with physical and mental fatigability, respectively, in age, sex, BMI-adjusted regression models ( $p$ 's<0.001), suggesting older adults can distinguish between physical and mental domains. Future work will explore how these constructs are distinct but related, and confirm the optimal proxy for the two fatigability subdomains.

#### ASSOCIATION OF WALKING ENERGETICS WITH AMYLOID STATUS: FINDINGS FROM THE BALTIMORE LONGITUDINAL STUDY OF AGING

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Higher energetic costs for mobility are associated with slow and declining gait speed. Slow gait is linked to cognitive decline and Alzheimer's disease (AD), but the physiological underpinnings are not well-understood. We investigated the cross-sectional association between the energetic cost of walking and amyloid status (+/-) in 174 cognitively unimpaired men and women (52%) aged 78.5±8.6 years. The energetic cost of walking was assessed as the average oxygen consumption (VO<sub>2</sub>) during 2.5 minutes of customary-paced overground walking. Amyloid status was determined from 11C-Pittsburgh compound B (PiB) positron emission tomography (PET) imaging. Average energetic cost of walking was .169±.0379 ml/kg/m and 30% of the sample was PiB+. In logistic regression adjusted for demographics, APOE-ε4, body composition and comorbidities, each 0.01ml/kg/m higher energy cost was associated with 12% increased odds of being PiB+ (OR=1.12; 95% CI:1.01-1.24). Inefficient walking may be a clinically meaningful physiological indicator of emerging AD-related pathology.

#### CORTICO-STRIATAL FUNCTIONAL CONNECTIVITY REFLECTS CHANGES IN SUBJECTIVE ENERGY AND TIREDNESS

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Subjective feelings of energy and tiredness may reflect different neural processes. Functional connectivity (FC) was measured in 272 HealthABC participants via resting state functional MRI in striatal-associative, striatal-limbic and striatal-sensorimotor networks. Subjective energy level (scored 1-10) and tiredness (tired/not-tired) during the prior month were collected via self-report from year 2 to year 10 (mean energy follow-up=8 years, tiredness follow-up=7 years). Participants who never reported being