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Frailty is increasingly recognised for its association with adverse health outcomes including mortality. However, various measures are used to assess frailty, and the strength of association could vary depending on the specific definition used. This umbrella review aimed to map which frailty scale could best predict the relationship between frailty and all-cause mortality among community-dwelling older people. According to the PRISMA guidelines, Medline, Embase, EBSCOhost and Web of Science databases were searched to identify eligible systematic reviews and meta-analyses which examined the association between frailty and all-cause mortality in the community-dwelling older people. Relevant data were extracted and summarised qualitatively. Methodological quality was assessed by AMSTAR-2 checklist. Five moderate-quality systematic reviews with a total of 374,529 participants were identified. Of these, two examined the frailty phenotype and its derivatives, two examined the cumulative deficit models and the other predominantly included studies assessing frailty with the FRAIL scale. All of the reviews found a significant association between frailty status and all-cause mortality. The magnitude of association varied between individual studies, with no consistent pattern related to the frailty measures that were used. In conclusion, regardless of the measure used to assess frailty status, it is associated with an increased risk of all-cause mortality.

FUNCTIONAL NEURAL UNDERPINNINGS OF INCREASED FALLS RISK

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Impaired cognition, especially in the domain of executive functions, is a major risk factor for falls in older adults. However, the underlying neural mechanism of the association between cognitive function and falls risk remains unclear. The current study compared the performance on mobility and cognitive assessments, and brain activation under Stroop task between fallers (>=2 falls in the past year) and non-fallers (0 or 1 fall in the past year). We found that during the incongruent condition of Stroop task, higher activation in precuneous, frontal and temporal areas was observed in fallers, while they showed comparable task performance as non-fallers. In addition, the contrast between congruent and incongruent conditions showed fallers exhibited increased activation in middle frontal region ($z>1.7$, $P<0.05$). Further, through mediation analysis, our data revealed that brain activation in temporal and frontal-paracingulate regions mediated the relationship between Montreal Cognitive Assessment and number of falls (confidence interval = 95%), after controlling for age and sex. Overall, our findings suggested that lower neural efficiency may be an underlying mechanism by which cognitive function is associated with falls risk.

LOSS OF ARNT LIMITS IMPROVEMENT IN PHYSIOLOGICAL PERFORMANCE FOLLOWING AEROBIC EXERCISE IN AGING

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Hypoxia signaling is essential for angiogenesis and metabolic regulation during exercise. Our previous study has demonstrated an age-related loss of ARNT resulting in limited muscle regeneration. To explore the role of hypoxia signaling in physiological performance in relation to aging, we generated a mouse model with skeletal muscle-specific knockout of ARNT (ARNT mKO). ARNT mKO and ARNT WT mice were subjected to a sedentary activity or treadmill running exercise regime at an increasing speed of 8-12 m/min for 40 minutes, three times weekly over the course of 8 weeks. ARNT levels was 3-fold lower in old mice compared to young. The exercised WT mice exhibited 52% greater increase over the sedentary group in exercise endurance as measured by the maximum running distance (490.92±154.28 vs 237.76±135.19m, $p < 0.01$). In contrast, ARNT mKO mice did not benefit from exercise (231.85±198.61 vs 167.27±136.56m, p=0.41). The maximum running speed was severely restricted in the trained ARNT mKO mice versus WT (16±1.63 m/min vs 26.67±2.45 m/min, $p < 0.001$). Cross-sectional area of myofibers increased significantly following exercise in WT mice (2270 vs 2960 □m2, p=0,015) indicating muscle hypertrophic response, while no change was observed in the ARNT mKO group (2101 vs 2378□m2, p=0,21). Further, exercise increased femoral artery blood flow by 41% in ARNT WT mice, but not in ARNT mKO mice (898.96±52.33 vs 802.86±48.43, p=0.20). These data suggest that ARNT is essential for physiological response to exercise

MEDITERRANEAN VERSUS WESTERN DIET EFFECTS ON CEREBRAL CORTICAL THICKNESS AND VOLUME IN CYNOMOLGUS MONKEYS

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Diet may influence the risk for cognitive decline and neurodegenerative disorders, including Alzheimer's disease (AD), but these relationships are difficult to study in humans. Cynomolgus macaques (Macaca fascicularis) are appropriate models for investigations of diet effects on the brain because, like humans, they are omnivorous, have complex central nervous systems, are susceptible to diet-induced diseases, and accumulate amyloid and tauopathies with age. Using structural magnetic resonance imaging, we examined diet effects on brain anatomy by measuring thickness and volume of several areas relevant to AD in 38 middle-aged females, at baseline and after Mediterranean or Western diet consumption for 36 months (equivalent to a 9-year follow-up in humans). Using repeated measures analysis, cortical thicknesses generally increased in the Western diet group. Western diets also resulted in increases in total brain volume and cortical gray matter and decreases in cerebrospinal fluid, white matter, and deep gray matter (striatum and thalamus) (all p's≤0.05). In contrast, thicknesses and volumes generally remained