This review presents findings on the role of female reproductive factors on longevity.A comprehensive systematic literature search was conducted using four electronic databases: OVID Medline, Web of Science, PubMed and Google Scholar from inception until May 2020 and restricted to English language articles that tackle the relationship between reproductive factors and longevity in its various definitions. Our search yielded a total of 306 articles. After screening based on the eligibility criteria,37 articles were included for review. The majority of studies were prospective and conducted in Western populations. The most consistent findings were between parity and increased longevity. The role of ages at menarche and menopause, premature menopause, as well as reproductive lifespan on longevity were not conclusive. Whether gender of offspring is related to maternal longevity is yet to be fully elucidated.Variations in findings are in the majority due to differentials in the definition of longevity as an outcome. Further longitudinal studies based in developing countries are needed to examine reproductive factors related to longevity.

A ROBOTIC SYSTEM FOR HIGH-THROUGHPUT AUTOMATED LIFESPAN AND PHENOTYPING ANALYSIS IN C. ELEGANS

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A goal of gerontology-related research is to develop therapies to improve the healthy period of life by understanding and targeting the molecular hallmarks of biological aging. Much progress has been made toward understanding the genetic and biochemical nature of these hallmarks through studies using simple invertebrate model organisms, such as the nematode Caenorhabditis elegans. Over the past decade, the identification of potential genetic and pharmacological modifiers of lifespan and age-related pathologies in C. elegans and other model organisms has yielded fruitful leads for follow-up investigation. However, such studies are typically time- consuming and labor-intensive. The goal of our work is to automate tasks that require frequent, repeated observations and hours of manual labor to collect and analyze lifespan, motility, and other behavioral data in C. elegans and other nematode models. The advent of affordable high-quality digital cameras, robotics systems, and 3D printers, as well as the decreasing financial and computational costs of image storage and processing, have allowed us to automate data capture and analysis on a large scale. To this end, our group recently developed a tool, we call the WormBot, consisting of an unbiased, high-throughput, automated robotic system and corresponding software, to perform genetic and pharmacological quantification of lifespan and health measures in C. elegans and related nematode species. We will report updates recently made to this system, including significant improvements to hardware, and present screening results from proteasome stimulator drugs known to reduce the accumulation of proteotoxic proteins linked to neurodegenerative diseases and aging.

ACARBOSE SUPPRESSES SYMPTOMS OF MITOCHONDRIAL DISEASE IN A MOUSE MODEL OF LEIGH SYNDROME.

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Mitochondrial diseases are pathologies characterized by impairment in mitochondrial function. Mitochondrial dysfunction is also a hallmark of the aging process. Rapamycin, a drug that increases lifespan and reduces the incidence of age-related pathologies in multiple models, increases survival and reduces the impact of neurological symptoms in a mouse model lacking the complex I subunit Ndufs4. Here we show that acarbose, another drug that extends lifespan in mice, suppresses symptoms of disease and improves survival of Ndufs4-/- mice. Unlike rapamycin, acarbose rescues disease phenotypes independently of mTOR inhibition. Furthermore, rapamycin and acarbose have additive effects on clasping and maximum lifespan in Ndufs4-/- mice. Acarbose rescues mitochondrial disease independently of glycolytic flux and Sirt3 activity by potentially remodeling the microbiome. This study provides the first evidence that the microbiome may rescue severe mitochondrial disease and proof of principle that biological aging and mitochondrial disorders are driven by common mechanisms.

AGE, SEX AND CEREBRAL MICROBLEED EFFECTS ON WHITE MATTER DEGRADATION AFTER TRAUMATIC BRAIN INJURY

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Mild traumatic brain injury (mTBI) affects white matter (WM) integrity and accelerates neurodegeneration. This study assesses the effects of age, sex, and cerebral microbleed (CMB) load as predictors of WM integrity in 70 subjects aged 18-77 imaged acutely and ~6 months after mTBI using diffusion tensor imaging (DTI). Two-tensor unscented Kalman tractography was used to segment and cluster 73 WM structures and to map changes in their mean fractional anisotropy (FA), a surrogate measure of WM integrity. Dimensionality reduction of mean FA feature vectors was implemented using principal component (PC) analysis, and two prominent PCs were used as responses in a multivariate analysis of covariance. Acutely and chronically, older age was significantly associated with lower FA ($F_{2,65} = 8.7$, $p < .001$, $\eta 2 = 0.2$; $F_{2,65} = 12.3$, $p < .001$, $\eta 2 = 0.3$, respectively), notably in the corpus callosum and in dorsolateral temporal structures, confirming older adults' WM vulnerability to mTBI. Chronically, sex was associated with mean FA ($F_{2,65} = 5.0$, $p = 0.01$, $\eta 2 = 0.1$), indicating males' greater susceptibility to WM degradation. Acutely, a significant association was observed between CMB load and mean FA ($F_{2,65} = 5.1$, $p = 0.009$, $\eta 2 = 0.1$), suggesting that CMBs reflect the acute severity of diffuse axonal injury. Together, these findings indicate that older age, male sex, and CMB load are risk factors for WM degeneration. Future research should examine how sex- and age-mediated WM degradation lead to cognitive decline and connectome degeneration after mTBI.