network (VAN) surpassed the 50% overlap threshold with 85% and 66% overlap respectively. Additionally, after controlling for multiple comparisons and age, the level of disruption to the VAN was significantly associated with poorer global cognition, as measured by the MoCA (p=.001). These novel findings identify the functional networks most affected by the presence of WMLs in older adults with CvD and suggest that the disruption to the VAN caused by WML load may underlie the deficits seen in cognition in this population.

PATTERNS OF WEIGHT CHANGE IN AGING AND DYING

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Little research has characterized the natural history of weight change in older adults. Different changes may occur during aging and dying. We analyzed 18 years of weight measures from a cohort of 736,361 Veterans, all of whom had died at age 70 or older. We produced summary measures that accounted for both chronological age and number of years before death. Several clear population-level trends appeared. (1) The average weight of the sample declined across all ages at a rate of about 0.18 BMI points per year. (2) Starting about seven years before death, the amount of loss began to accelerate, reaching a decline of 0.75 BMI points in the year before death. (3) Changes in weight relative to years of remaining life were independent of chronologic age. People who died at age 70 experienced, on average, the same type and duration of terminal decline as did those who died at age 95. (4) The dying process involved a cumulative loss of about 1.3 BMI points. (5) The distribution of weights during advancing age both declined and narrowed. (6) Disproportionate deaths occurred at the lower BMI ranges (below a BMI of 24), and especially below 18, regardless of age. (7) The finding in #5 is explained by the entire cohort losing weight, with death of the thinnest members. These findings argue for examining survival time in studies of weight change. They indicate that weight loss may be a natural part of dying, rather than a risk factor for it.

RESTRICTED MEAN SURVIVAL TIME IN ACTION TO CONTROL CARDIOVASCULAR RISK IN DIABETES (ACCORD) BLOOD PRESSURE

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Background: Restricted mean survival time (RMST) provides mean time lost or gained by an intervention. This may be a more intuitive way to understand treatment effect. Objective: To determine overall and subgroup treatment effects from blood pressure targets in older adults with diabetes. Methods: We analyzed the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial data. Our outcome was cardiovascular disease free survival. We measured 5-year RMST (days) between standard and intensive blood pressure control, and compared the difference by age (≥70 or <70 years old) and glycemic control (standard vs. intensive). Results: Over 5 years, those with intensive treatment lived, on average, 1716 days compared to 1714 days with standard treatment, with a RMST difference of 1.3 days (95% confidence interval, -22.1, 12.4). Among adults ≥70 years old, compared to standard treatment, intensive treatment resulted in an additional 13.6 (95% CI, -43.2, 70.3) days, where the difference was -0.5 (-20.8, 19.7) days for those aged <70 years old (p-for-interaction=0.673). Compared to standard treatment, intensive treatment resulted in 28.1 (0.4, 55.9) more days for those assigned to standard glycemic control, but it appeared to result in 25.2 fewer days (-52.3, 1.9) for those assigned to intensive glycemic control (p-for-interaction=0.007). Discussion: The benefit of intensive treatment over standard treatment varies by age and glycemic control. RMST difference may allow for more intuitive and personalized weighing of benefits and risks of intensive blood pressure control.

ROLE OF GENETIC INTERACTIONS IN ALZHEIMER'S DISEASE: LESSONS FROM LONG LIFE FAMILY STUDY (LLFS)

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Experimental and clinical studies of Alzheimer's disease (AD) provide plentiful evidence of AD heterogeneity and involvement of many interacting genes and pathways in regulation of AD-related traits. However, detailed mechanisms of genetic interactions (GxG) involved in AD remain largely unknown. Uncovering hidden patterns of such interactions from human data will help better understand the nature of AD heterogeneity and find new targets for AD prevention. In this paper, we applied a newly developed method of evaluating joint GxG effects on AD to analysis of the Long Life Family Study data. The analysis included several steps: (i) selecting candidate genes from stress response pathways that are thought to be involved in AD; (ii) estimating interaction effects of SNP-pairs on AD risk, and selecting the top interacting SNPs; (iii) running GWAS-like interaction analysis for SNP-pairs, with one SNP fixed; (iv) using characteristics of the detected SNP-pairs interactions to construct the SNP-specific Interaction Polygenic Risk Scores (IPRS); and (v) evaluating the effects of IPRSs on AD. We found that SNP-specific IPRS have highly significant effects on AD risk. For most SNPs involved in the significant interaction effects on AD, their individual effects were statistically not significant. Male and female analyses yielded different subsets of the top interacting SNPs. These results support major role of genetic interactions in heterogeneity of AD, and indicate that AD mechanisms can involve different combinations of the interacting genetic variants in males and females, which may point to different pathways of resistance/response to stressors in two genders.

TORQUE AND VELOCITY DEPENDENCE OF MUSCLE FATIGUE IN AGING

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