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Adiposity and Brain Health

Adipose tissue influences health of both central and peripheral nervous systems via neuroendocrine and vascular mechanisms. Body mass index (BMI), body weight and waist circumference are common measures of overweight and obesity in epidemiologic studies. Neuroepidemiological associations between the adiposity phenotype by neurological outcome vary depending on when and how during the human life course adiposity is measured and age and stage of neuropathological and clinical outcomes onset and progression. Secular changes in environment and socioeconomic and cultural factors globally, also influence observed associations. Over the adult life course, overweight and obesity during middle age are associated with higher risk for late-life Alzheimer's Disease and Related Dementias (ADRD) and underlying neuropathologies. However, there is often observed an 'obesity paradox'. BMI and body weight increase until approximately age 70 years, when there is often observed an inflection point, and BMI and body weight decrease. In later life, higher BMI is subsequently protective for AD, since AD is often characterized by lower and/or greater declines in body weight. Some studies observe that possession of the APOE ϵ 4 allele is associated with steeper BMI and body weight decline, irrespective of whether dementia develops. Observations in susceptible populations, including HIV-infected adults and indigenous elders, may differ. Risk and/or prognosis of other neurological outcomes in association with adiposity include Parkinson's disease, migraine, multiple sclerosis, peripheral neuropathies, and late-onset Huntington's Disease.

Acknowledgements

NIH/NHLBI, 5U01HL146202-03, 3U01 HL146202 02S; NIH/NIAID U01 1A131834, AI031834-18S1; Swedish Council for Working Life and Social Research 2013-2496, 2013-2300; University of Arizona Faculty Seed grant; Empire Clinical Research Investigator Program; European Union FP7 project Grant Agreement N° 211696; Swedish Research Council; NIH/Native American Research Centers for Health; LUA/ALF Västra Götaland; Hans-Gabriel & Alice Trolle-Wachtmeisters Foundation for Medical Research; NIH/NIA.

Abstract References

1. Macaluso F, Weber KM, Rubin LH, Dellinger E, Holman S, Minkoff H, Keating S, Merlin LR, Gustafson DR. Body mass index and circulating leptin are related to cognitive performance over 10 years in women with and without HIV infection. *J Clin Endo Metab*, 2022;107:e1126-e1135.
2. Gustafson DR, Bäckman K, Scarmeas N, Stern Y, Manly JJ, Mayeux R, Gu Y. Dietary fatty acids and risk of Alzheimer's Disease and Related Dementias. Observations from the Washington Heights - Hamilton Heights - Inwood Columbia Aging Project (WHICAP). *Alzheimers & Dementia*, 2020;16:1638-1649.
3. Arnoldussen IAC, Gustafson DR (co-first authors), vanLeijzen EMC, deLeeuw FE, Kiliaan AJ. Adiposity is related to cerebrovascular and brain volumetry outcomes in the RUN DMC Study. *Neurology*, 2019;93:e864-e878.
4. Rubin LH, Gustafson D (co-first authors), Hawkins KL, Zhang L, Jacobson LP, Becker JT, Munro CA, Lake JE, Martin E, Levine A, Brown TT, Saktor NC, Erlandson KM. Midlife adiposity predicts cognitive decline in the Multicenter AIDS Cohort Study (MACS). *Neurology*, 2019;16;93:e261-e271.
5. Gachupin F, Romero M, Ortega W, Jojola R, Hendrie H, Torres Sr EP, Lujan F, Lente MA, Sanchez B, Abeita F, Abeita U, Lente B, Teller V, Gustafson DR. Cognition, depressive symptoms and vascular factors among Southwest Tribal elders. *J Ethnicity Disease*, 2016;26:235-244.
6. Bäckman K, Joas E, Waern M, Östling S, Guo X, Blennow K, Skoog I, Gustafson DR. 37 Years of Body Mass Index and Dementia: Effect Modification by the APOE Genotype: Observations from the Prospective Population Study of Women in Gothenburg, Sweden. *J Alzheimers Dis*, 2015;48:1119-27.
7. Kiliaan AJ, Arnoldussen IA, Gustafson DR. Adipokines: a link between obesity and dementia? *Lancet Neurol*, 2014;13:913-23.
8. Besser LM, Gill DP, Monsell SE, Brenowitz W, Meranus D, Kukull W, Gustafson DR. Body mass index, weight change, and clinical progression in Mild Cognitive Impairment and Alzheimer's Disease. *Alz Dis Assoc Disorders*, 2014;28:36-43.
9. Gustafson D, Ongaro F, Meggiolaro S, Antuono P, Forloni GL, Albani D, Gajo GB, De Angeli S, Zanardo A Siculi M, Siculi G, Muffato G, Gava N, Regini C, Gallucci M. Body mass index, cognition, disability, APOE genotype and mortality: the "TREVISIO LONGEVA (TRELONG)" Study. *Am J Geriatric Psych*, 2012;20:594-602.
10. Gustafson DR, Rothenberg E, Blennow K, Steen B, Skoog I. An 18-year follow-up of body mass index and risk for Alzheimer's Disease. *Arch Internal Med*, 2003;163:1524-1528.