



### Metabolic profile and declining cognitive function

A cohort study suggests that metabolic abnormality is a risk factor for cognitive decline with increasing body mass index.



**Overview:** Obesity is typically accompanied by unfavourable metabolic profiles, such as high blood glucose, adverse lipid levels, and elevated blood pressure. However, the concept of metabolically healthy obesity has been used to describe people with a BMI of 30 kg/m<sup>2</sup> or more and an otherwise healthy metabolic profile. Research suggests that the metabolically healthy obesity phenotype may not be associated with increased risk of cardiovascular disease.

Studies have suggested that being overweight or obese, particularly in mid-life, are risk factors for dementia. However, little is known about the impact of metabolically healthy obesity on cognitive function.

**Current advice:** NICE has a clinical guideline covering the [prevention, identification, assessment and management of overweight and obesity in adults and children](#). NICE guidance on [dementia](#) recommends that health professionals review and treat vascular and other modifiable risk factors for dementia, such as smoking, excessive alcohol use, obesity, diabetes, hypertension and raised cholesterol levels, in people who are middle-aged and older.

**New evidence:** A prospective cohort study of civil servants participating in the [Whitehall II cohort study](#) examined BMI, metabolic status and cognitive function ([Singh-Manoux et al. 2012](#)). This analysis included data on 6401 adults (71.2% men), aged 39–63 years, over a 10-year period from 1997. Of these, 52.7% were a healthy weight, 38.2% were overweight, and 9.1% were obese. Metabolic abnormality was defined as 2 or more of high triglycerides, cholesterol or blood glucose or hypertension, or drug treatment for any of these conditions. Overall, 31.0% of all participants (n=1985) and 60.1% (n=350) of obese participants had metabolic abnormalities.

A global cognitive score was calculated from the results of assessments of reasoning, short-term verbal memory and verbal fluency. For people classed as metabolically normal, the change in global cognitive score was not significantly different between those who were normal weight, were overweight, or were obese (10-year decline of -0.40, -0.42, and -0.42 respectively). However, for people classed as metabolically abnormal, a significant difference was seen (10-year decline of -0.40, -0.43, and -0.49 respectively, p=0.03). The authors concluded that the fastest cognitive decline was seen in people with both obesity and metabolic abnormality.

**Commentary:** "Mid-life obesity has consistently been associated with increased risk of dementia. In contrast, this study reported a lack of association between obesity and risk of cognitive decline in people who had no metabolic abnormalities. These results confirm the limitations of BMI alone as a predictor of cognitive risk. For example, waist circumference may have been a better predictor of cognitive decline than BMI because it is more strongly associated with visceral adiposity. Additionally, use of prescription drugs to treat metabolic abnormalities may have reduced the cognitive and

cardiovascular risks. Further sensitivity analysis could indicate whether 10-year cognitive decline differed between people on treatment for metabolic abnormalities and those with untreated metabolic abnormalities.

"The observed link between increased weight and poor cognitive function has only started to be translated into clinical trials investigating the impact of weight modification and obesity prevention programmes on cognitive outcomes. Recent meta-analyses have reported beneficial effects of calorie restriction and physical activity on cognitive function. However, studies have overall been characterised by limited power, short duration and large heterogeneity that has prevented any attempt to develop specific recommendations to modify the risk of cognitive decline associated with increased weight". – **Dr Mario Siervo, Lecturer in Nutrition and Ageing, Human Nutrition Research Centre, Institute for Ageing and Health, Newcastle University**

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