# Neck Circumference, Brain Imaging Measures, and Neuropsychological Testing Measures

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*Background:* Perivascular fat may have direct effects on local vascularity. Neck fat is associated with carotid intimal thickness, a predictor of brain aging outcomes. This study investigated whether neck circumference, an estimation of neck fat, has unique associations with brain aging outcomes. *Methods:* The study sample (n = 2082, 53.5% women, mean age 60.9 years) was derived from Framingham Heart Study participants with brain magnetic resonance imaging (MRI) and neuropsychological (NP) test measures. Multivariable-adjusted regressions examined cross-sectional associations of neck circumference with brain MRI and NP test measures. Models were also constructed with waist circumference and body mass index (BMI) as exposures. *Results:* A 1 standard deviation (2.8 cm [women]; 2.9 cm [men]) increment in neck circumference was associated with lower total cerebral brain volume ($\beta = -.22$, $P = .0006$) and lower frontal brain volume ($\beta = -.55$, $P < .0001$). However, a similar association was observed for both waist circumference and BMI. There were no associations between neck circumference and NP test measures after full covariate adjustment. *Conclusions:* There were no unique associations between neck circumference and brain MRI or NP measures. Consistent with prior observations, all adiposity measures showed associations with more adverse brain MRI and NP measures, suggesting a global association of generalized adiposity. **Key Words:** Epidemiology—population studies—cognition—adiposity.


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## Introduction

Obesity is associated with increased risk for all-cause dementia, vascular dementia, and Alzheimer's disease.[1] Increased body mass index (BMI) is associated with an increased incidence of dementia and increased cerebral atrophy.[2,3] Similarly, waist circumference is independently associated with dementia.[4] One theory for the wide-ranging systemic associations of global adiposity on cognitive function is the possible role of adipokines in the progression of dementia.[5]

The local effects of adipose tissue on cognitive function are less well characterized. Increased neck circumference, an estimation of upper body subcutaneous fat, has been associated with an increased internal and common carotid artery wall intima–media thickness.[6] This association persisted after adjustment for BMI, suggesting it is not solely due to global adiposity but may have been in part due to a local effect of upper body subcutaneous fat.[6] Additionally, other studies have found associations between carotid artery intima–media thickness and stroke incidence, a common component of vascular cognitive impairment, as well as decreased total brain volume and decreased cognitive function.[7,8] However, it has not been investigated if the potential local association of neck fat on carotid health extends to an association of neck fat and cognitive impairment consistent with vascular etiology.

Therefore, the goal of our study was to investigate if there is an association between neck circumference with common markers of brain tissue damage and cognitive function. We hypothesized that because of the local effects of subcutaneous fat on neck vasculature, we would observe a lower total cerebral brain volume and frontal brain volume, but no association with non–vascular-derived sizes such as hippocampal volume. Additionally, we hypothesized that we would observe an association between neck circumference and decreased cognition particularly for cognitive tasks associated with frontal lobes such as executive function.

## Methods

### Study Participants

The sample is composed of Framingham Heart Study Offspring participants who were initially recruited in 1971.[9] These participants are the offspring and offspring's spouses of the original community-based cohort who were recruited in 1948.[9,10] Participants volunteer for regular examinations with the study.

Participants in this sample attended the seventh examination cycle from 1998 to 2001 as well as follow-up neuropsychological (NP) testing and a brain magnetic resonance imaging (MRI). A total of 3539 participants provided informed consent and attended the examination. The following hierarchical exclusions were made: (1) missing neck circumference, waist circumference, and/or BMI measures (n = 252); (2) missing MMSE (mini–mental state examination) score (n = 9); (3) missing brain MRI and/or NP testing measures (n = 1112); and (4) history of prevalent dementia, stroke, or other neurological conditions at the time of the brain MRI or NP testing (n = 74). The final sample size was 2082.

### Measurements of Neck Circumference, Waist Circumference, and BMI

Neck circumference was measured just below the laryngeal prominence with a tape measure to the nearest quarter inch. Waist circumference was measured to the nearest quarter inch at the level of the umbilicus. BMI was calculated as weight in kilograms divided by height in meters squared. Participants were weighed on a regularly calibrated Detecto scale (Worchester Scale Co Inc) in only gowns and socks. Weight was recorded to the nearest pound.

### Brain Imaging Measurements

The method for brain MRI procedure and subsequent image analysis used for this study has been detailed previously.[11] To summarize, a 1-T field strength Siemens Magnetom scanner (Siemens Medical, Erlangen, Germany) was used to obtain 4-mm contiguous slices with a double spin-echo coronal imaging sequence. Total cerebral brain volume, frontal brain volume, hippocampal volume, and white matter hyperintensity volume were measured using a validated protocol and program which has been described previously.[12,13] Briefly, volumes besides white matter hyperintensity were determined via manual tracing and automated removal of CSF on a customized computer program with high intrarater and inter-rater reliability.[12] For all brain MRI scans, we used the same MRI scanner, same facility, and same MRI protocol. Additionally, all scans were analyzed by the same lab.

White matter hyperintensity was differentiated from normal parenchyma in a multistep process in which area intensities 3.5 standard deviations above the mean were defined as white matter hyperintensities. This process has been described in more complete detail and validated elsewhere.[12] Extensive white matter hyperintensities were defined as having a 5-year age-group specific z-score greater than 1.

### NP Testing Measurements

Participants in this study underwent standardized NP testing as has been previously described.[14] Traditional scoring was used to determine the standard quantitative scores for each test. Error responses were also factored into scoring. The test battery included subtests of the Wechsler Memory Scale: Logical Memory (immediate and delayed recall) and Visual Reproductions (immediate and delayed recall).[15] Only the delayed recall results were used