

# Midlife Obesity and Cortical Atrophy

## A lipid-related process?

## A path to dementia?

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# NeuroCHARGE project - PROTOCOL

## Step 1: Association between body adiposity and 34 cortical volumes

Age

Youth: <35 yrs

Midlife: 35-65 yrs

Later life: >65 yrs

Body adiposity

Underweight  
BMI < 20 kg/m<sup>2</sup>

Normal weight, overweight, and obesity  
BMI ≥ 20 kg/m<sup>2</sup>

Free of:

- Brain morphological abnormalities (e.g., cysts, brain tumors)
- Neurodegenerative/brain diseases (dementia, stroke, multiple sclerosis [if known])

Data

Body adiposity

Body mass index

Waist circumference (adjusted for height)

Waist to hip ratio

Cortical volume (thickness, surface area)

34 cortical regions (FreeSurfer)

Intra-cranial volume (ICV)

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Primary: Sex-, APOE4-, ancestry-, and ethnicity-pooled

Basic Model

Cortical volume ~ adiposity + age + age<sup>2</sup> + age-difference + genotype PCs + ICV + cohort-specific covariates + sex

Full Model

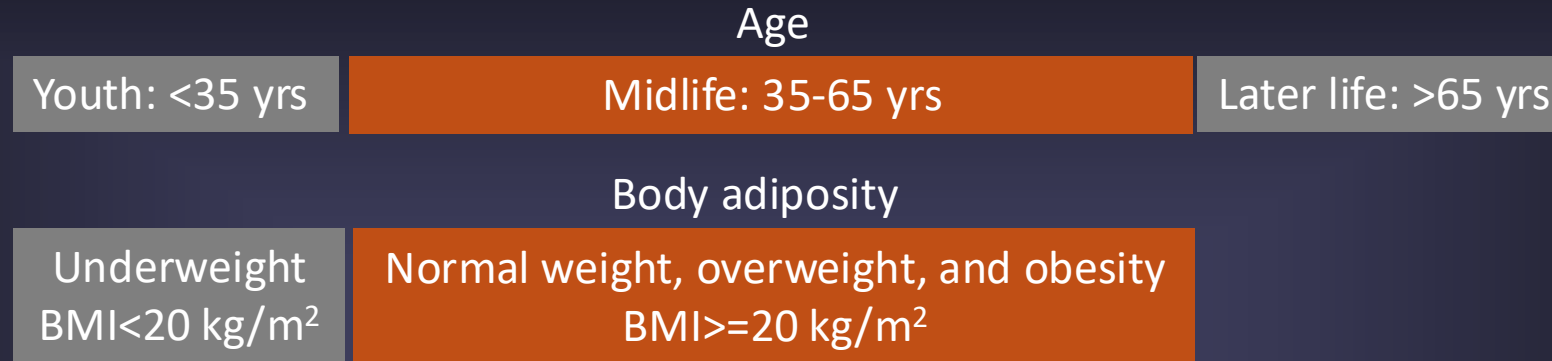
Cortical volume ~ adiposity + age + age<sup>2</sup> + ICV + age-difference + genotype PCs + cohort-specific covariates + smoking + hypertension + T2D + sex

Volume and adiposity will first be adjusted for age, ICV (for cortical volume), and/or height (for waist circumference) within each sex separately, to account for any sex-specific associations.

Regional association estimates obtained in this step will be used for *virtual cortical lipidomics*

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### Secondary:

- (1) Sex-, *APOE4*-, ancestry-, ethnicity-, age-, bmi-stratified
- (2) Sex-, *APOE4*-, ancestry-, and ethnicity-pooled, additionally adjusting for ethnicity
- (3) Sex-, *APOE4*-, ancestry-, and ethnicity-pooled analyses of cortical cortical surface area and thickness