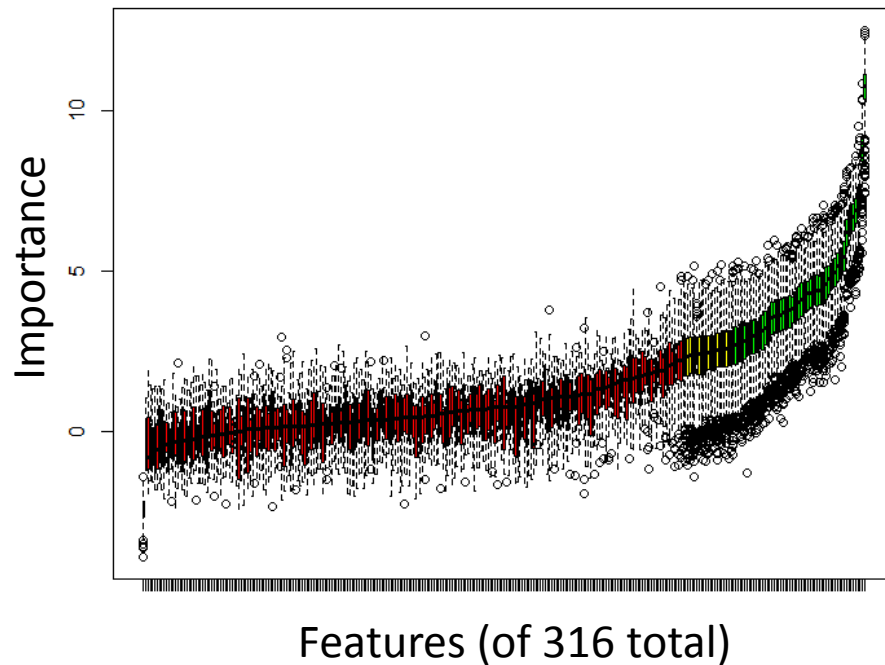


**Figure S1. Effect of removing specific metabolic parameters on metabolic brain age estimations.** (A) Predicted metabolic brain age was calculated using random forest regression with bias correction 10 times from either the whole data set, or the data set with a specific parameter removed (AG, CMRGlc, CMRO2, or CBF). Removing AG had the most significant effect on reducing the accuracy of the predicted metabolic brain age, but the change in accuracy was minor. (B) Differences between male and female metabolic brain age was calculated 10 times each from either the whole data set or with a specific parameter removed. While female metabolic brain age remained younger than males in all instances, removing CMRGlc reduced this difference while removing CBF increased it.

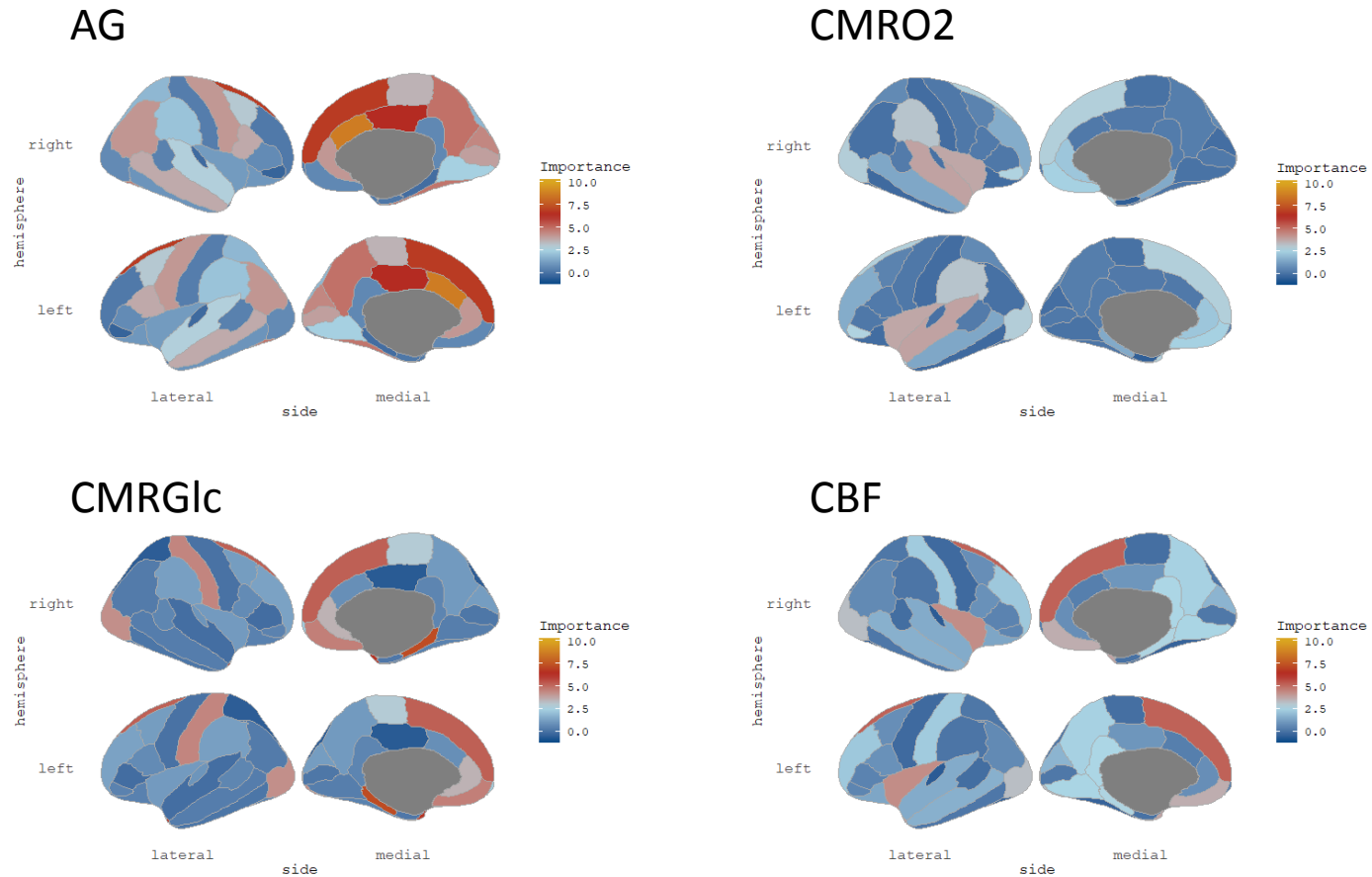


#### Select features confirmed important by Boruta package (v5.3.0) in R

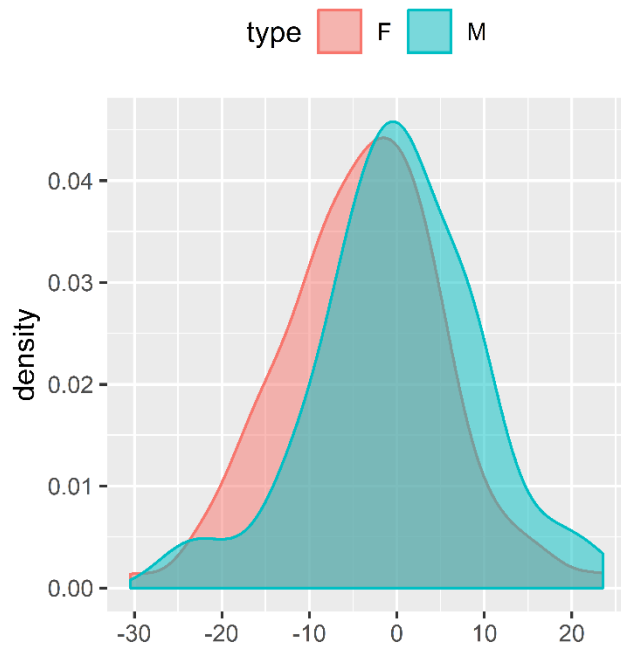
AG	Caudal anterior cingulate, superior frontal, posterior cingulate, precuneus, fusiform, cuneus, inferior parietal, rostral anterior cingulate, and precentral gyri
CMRGlc	Parahippocampal gyrus, pallidum, temporal pole, superior frontal, medial orbitofrontal, lateral occipital gyri, and superior temporal white matter
CMRO2	Cerebellum, pallidum
CBF	Pallidum, thalamus, precentral, superior frontal, insula, caudate, and white matter of several regions including frontal lobe, superior parietal, and inferior temporal regions

#### Figure S2a. Important features for random forest estimation of metabolic brain age.

The Boruta package (v5.3.0) as implemented in R was performed on the normalized brain metabolism data (79 regions x 4 metabolic parameters). Of the 316 total features, the package identified 59 features as 'confirmed' (green) as being important and another 20 as 'tentatively' (yellow) important. The confirmed features include those involving all 4 metabolic features, including AG in cingulate and superior frontal regions, CMRGlc in the temporal lobes, and CBF in the basal ganglia having among the highest importance values. The table shows regions with a mean importance value > 4.0.

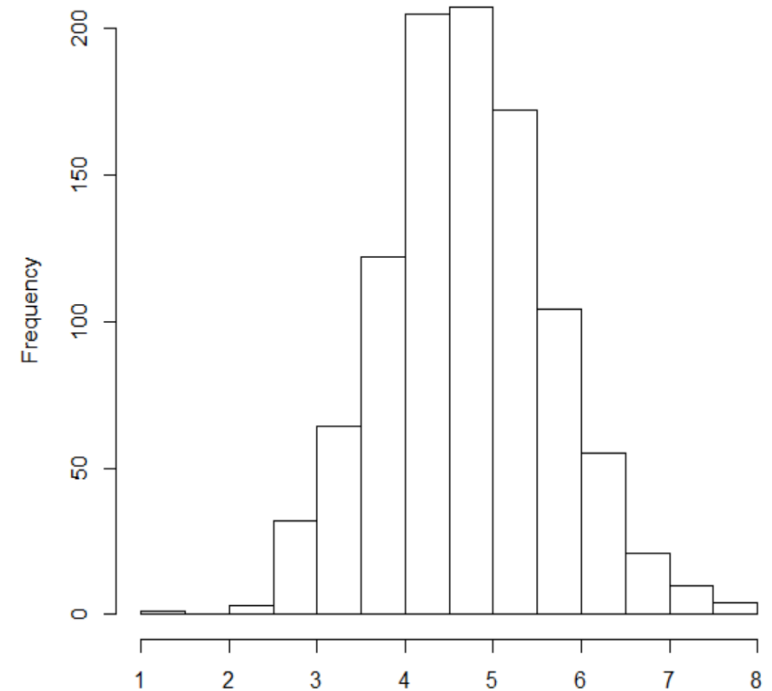


**Figure S2b. Important features for random forest estimation of metabolic brain age.** Results from the Boruta package regarding regional importance are mapped to cortical regions based on the Desikan-Killiany Atlas.



**A**

Actual age – metabolic brain age (y)



**B**

Male metabolic brain age – Female metabolic brain age

**Figure S3. Differences between female and male metabolic brain age.** (A) Histogram analysis of female and male actual – metabolic brain age demonstrates a leftward shift for females as compared to males. (B) The difference between male and female metabolic brain age was tested on 1000 permutations of the data set where 60 of the 79 regions were randomly chosen, to determine whether a small subset of regions drove the sex differences in metabolic brain age. In all 1000 cases, mean male metabolic brain age was greater than that for females (mean difference 4.7 years).