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Deep learning of brain MRI reveals sex and ethnicity-dependent brain aging led by metabolic syndromes

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Background

The prevalence of metabolic syndromes including obesity, hypertension, and diabetes has increased worldwide and are associated with several important aspects of brain aging, such as cortical atrophy, white matter demyelination and cognitive impairment [1]. While it is largely documented that association between metabolic syndromes and brain aging vary depending on sex [2][3].

Brain age can be reliably estimated by machine learning from aging-related structural brain MRI [4]. The difference between an individual's predicted and chronological age, namely relative brain age (RBA), is considered a marker of aging-related brain diseases [5]. In this study, we aimed at investigating interaction of sex and ethnicity with brain aging led by metabolic syndromes.

Dataset

two large-scale ethnically distinctive datasets – UK biobank (UKBB) dataset and Korea Health Promotion Center of the Samsung Medical Center (KORHPC) dataset. 7373 subjects from UKBB (99% European Caucasians, 3766 controls, 3607 with metabolic syndromes including diabetes, hypertension and obesity) and 3208 subjects from KORHPC (100% Asians, 1325 controls, 1883 with metabolic syndromes) were selected for analyses (Fig 1).

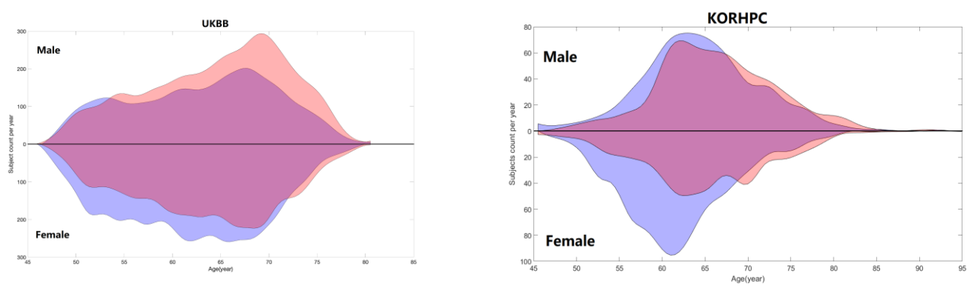

Fig. 1. Age distribution for two datasets

Methods

For each subject, white surfaces and pial surfaces were reconstructed using the CIVET pipeline [6]. Cortical thickness and gray/white matter intensity ratio [7] were measured on the cortical surface at 1284 vertices using the icosahedron down-sampling to save computational time.

Graph-convolutional networks (GCNs) [8][9] have been applied to predict the brain age underlying graph structure of the data like features mapped on the cortical surface. 70% of controls from the two datasets were randomly selected as for training/validation of GCN models. The rest 30% of controls and all subjects with metabolic disorders were used for testing GCN models and group comparison.

To avoid the different convergence of training GCNs due to GCN's random initialization of graph configuration [8], we performed 100 separate 5-fold cross validations. We produced the relative brain age (RBA) for the subsequent analysis by averaging each RBA generated from 5 folds x 100 times = 500 models.

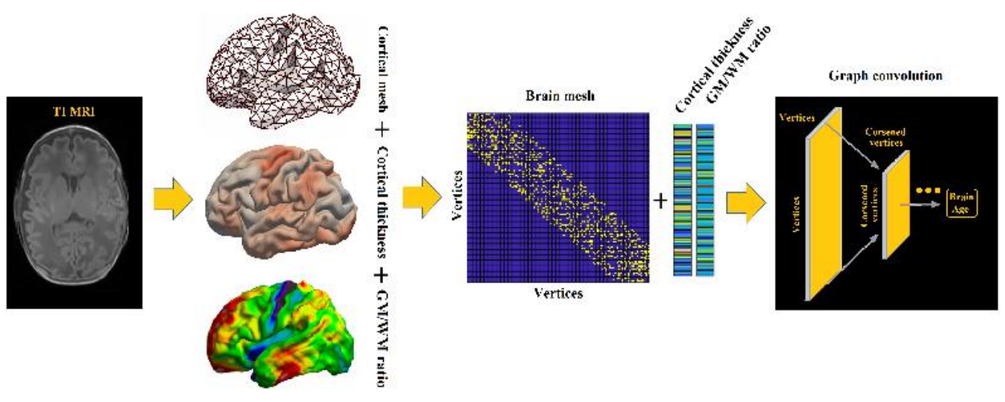

Fig.2. Brain age prediction pipeline using GCN

Results

1), The prediction accuracy for UKBB (MAE: 3.87±2.41 years) and KORHPC (MAE: 3.97±3.01 years) are almost equal.

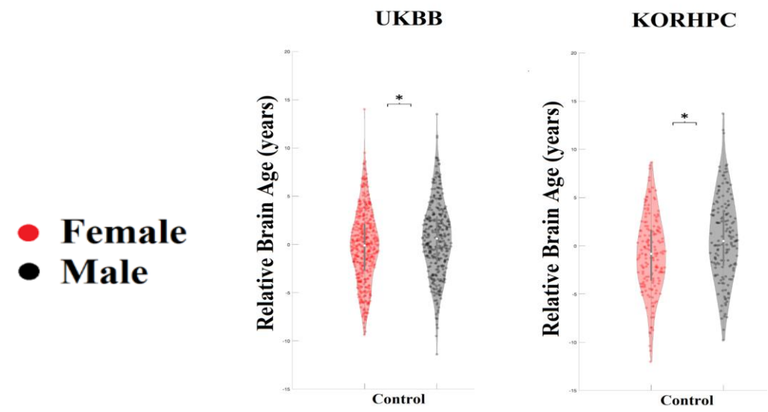

Fig.3. Sex difference of RBA in controls

2), 2x2 (ethnicity x sex) ANOVA Showed significance in gender (p <0.001), but not ethnicity and interaction (ethnicity x sex;)

3), For all metabolic syndrome groups showed older brains relative to controls (corrected p < 0.001; see table below).

Table 1. RBA in metabolic syndromes compared to controls

	UKBB			KORHPC		
	Diabetes	Hypertension	Obesity	Diabetes	Hypertension	Obesity
RBA vs control (years)	**+2.18**	**+1.01**	**+0.77**	**+1.43**	**+0.76**	**+1.02**

To investigate the ethnicity and gender differences in the effect of metabolic syndromes on brain aging, 2x2 between-subjects (ethnicity x gender) ANOVA was conducted on RBA for each syndrome group. Effects of diabetes (RBA = +0.62 years), hypertension (RBA = +1.05), and obesity (RBA = +1.56) on brain aging were significantly larger in males compared to females (p < 0.01). Effects of diabetes on brain aging was significantly larger in UKBB (RBA = +0.75) than KORHPC (p = 0.029). No other effects were found for all three syndromes.

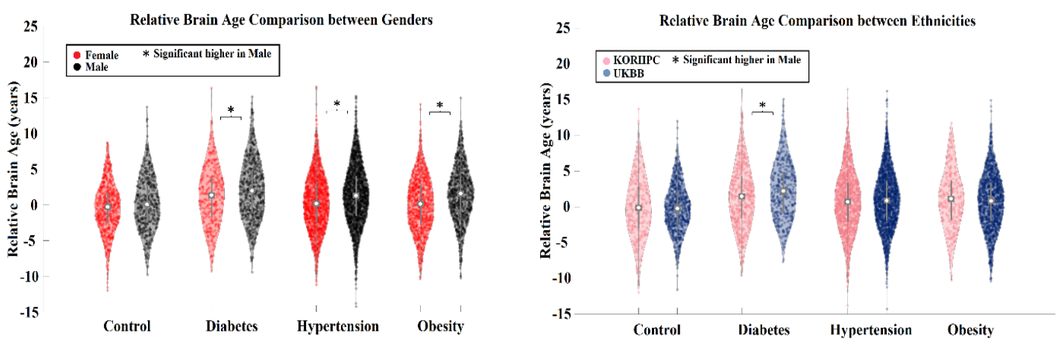

Fig. 4. Sex and ethnicity difference of RBA in metabolic syndromes

Conclusion

By analyzing large, multiethnic cohort data, we revealed that men in all three types of metabolic syndromes exhibited higher RBA than women, which has not been reported consistently in previous studies [2]. Our observation that brain aging in diabetic Caucasians were faster than Asians is novel. One caveat to note is whether this finding would be led partly or fully by difference in the prevalence of diabetes type I and II between the two ethnic datasets, which we did not consider in our statistical analysis.

Reference

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