

Regional Brain Age Measures Based on Convolutional Neural Networks (CNNs)—Symmetry Properties and Associations with Fluid and Crystallized Intelligence

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Abstract—By applying deep learning on 3D MR images, global brain age measures have been formulated by predicting the chronological age. However, little attention has been paid to regional brain age measures, which may capture the cognitive functions supported by individual brain regions. Using a sample of 1,703 T1-weighted images from the Human Connectome Projects (HCP-Young adult and HCP-Aging), we constructed 3D convolutional neural networks to estimate the regional brain ages of 18 cortical regions (9 on each cerebral hemisphere). Two hypotheses were tested: (1) on the cerebral cortex, there are higher associations of regional brain ages between homotopic than non-homotopic region-pairs; and (2) regional brain ages are directly associated with both crystallized and fluid intelligence even after chronological age is factored out. Three methods were implemented to ameliorate the “regression to the mean” (RttM) problem, ubiquitous in brain age studies, including Cole’s method, de Lange’s method, and our proposed “percentile matching” method, in which the prediction of the testing data is corrected for by mapping the distributional properties of the predicted value and ground truth using the validation data. While our results supported both hypotheses and confirmed the desirable symmetry and association properties, consistent evidence was found only when the regional brain ages were corrected for by either Cole’s method or the percentile matching method. Between these two methods, the latter method yielded smaller mean absolute error and root mean square error, along with larger Spearman’s correlation. Our results highlight the potential of regional brain ages and the percentile matching method in brain age research.

Clinical relevance—Regional brain ages exhibit symmetry properties and associations with cognitive functions, and they may represent promising biomarkers of brain ageing.

I. INTRODUCTION

Neuroimaging-based brain age prediction is a promising clinical application of deep learning [1], [2], [3], [4]. Taking one or multiple magnetic resonance (MR) images (T1-weighted, T2-weighted, diffusion-weighted, etc.) from an

individual as input and the chronological age as ground truth, the deep learning regression models output a predicted age, to be taken as the brain age (e.g., [5]). The difference between the brain age and chronological age, known variously as the brain age delta/gap or predicted age difference, can inform aspects of the disease development of individuals [2], [6], [7], suggesting its potential in personalized medicine [8]. Thus far, the vast majority of brain age studies estimated only global brain age measures. However, such global brain age measures have provided limited sensitivity towards brain functions, severely limiting their clinical utility. In fact, a recent study demonstrated that brain age measures do not capture fluid intelligence in older individuals above and beyond chronological age [9].

Only a limited number of studies have computed regional brain age measures (with the chronological age still taken as the ground truth). For example, one study has explored a similar idea termed “brain structure age (BSA)”, which was obtained by the following major steps: (1) segment the whole brain into a large number (125) of overlapping sub-volumes; (2) use a U-Net to calculate a brain age for each sub-volume; (3) a voxel-wise brain age map was obtained by averaging the brain age across the overlapping sub-volumes; (4) a local BSA was finally computed by simple averaging over each anatomically defined region of interest [7]. However, there has been little indication on whether such regional brain age measures can capture the process of cognitive ageing.

In the present study, two datasets from the Human Connectome Project (HCP) were employed to examine the hypothesis that regional brain age measures based on structural T1 MR images are associated with cognitive functions, which can be subdivided into two broad categories in fluid and crystallized intelligence [10]. Our method proposed here is conceptually simple. In brief, based on individualized FreeSurfer segmentation, the structural T1-weighted image of each individual was divided into a desirable number of anatomical regions by masking the original images. The masked images were then used to train a regional brain age model, in the same way that the unmasked images were used to train a global brain age model. This idea is similar to patch-based approaches proposed in previous studies [7], [11], [12], [13], with the major difference being that anatomical details are incorporated to the processing pipeline earlier, which results in more interpretable regional brain age measures [14].

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Towards establishing that structure-based regional brain age measures can capture the individual differences in cognitive ageing, we sought to test whether such measures exhibit certain desirable characteristics, namely, symmetry properties and associations with cognition. Firstly, homotopic regions, which refer to a pair of geometrically corresponding regions present in the opposite cerebral hemispheres (such as the left and right inferior frontal gyrus), are structurally and functionally connected even though they do not always subserve the exact same function [15]. Accordingly, ageing is expected to drive homotopic regions more similarly than non-homotopic regions. If this hypothesis is true, then on the cerebral cortex, the regional brain age measures would manifest certain symmetry, such that the associations of regional brain ages between homotopic region-pairs will tend to be stronger than non-homotopic region-pairs. Secondly, it is plausible that regional brain age measures can better account for individual variations in cognitive ageing than their global counterparts; however, this hypothesis has not yet been tested. As such, the present study also tested whether regional brain ages are directly associated with both crystallized and fluid intelligence even after chronological age is factored out.

In testing the two hypotheses above, it was observed that their extent of experimental support received depended on how the “regression to the mean” (RttM thereafter) problem was corrected for. This problem is well-recognized for regression problems, and refers to the overestimation and the underestimation of the predicted values at the two ends of the variable being predicted [16]. Within the brain age literature, to tackle this problem, the predicted values are adjusted using some correction formulae, such as Cole’s formula [3] and de Lange’s formula [17]. Both formulae were originally proposed to estimate the chronological age that would have corresponded to the resultant predicted regional brain age, through a simple linear regression. However, neither method is foolproof. For example, whether Cole’s formula can ameliorate the problem depends on the goodness of fit between the predicted value and the ground truth. In case of a relatively poor fit, the application of Cole’s formula will increase rather than reduce the mean absolute error (e.g., [5]). Regarding de Lange’s formula, it has also been recently demonstrated by the original proponent that it would yield artificially good MAE even for very poor models [18]. As such, a new method referred to as “percentile matching” was proposed in the present study to correct for RttM problem. In brief, this method achieved the same goal of estimating the relationship between the predicted value and the ground truth by using their distributional properties (Section II-G).

II. METHODS

A. Datasets

The dataset comprised the preprocessed MRI data from HCP-Young adult (HCP-YA) and HCP-Aging. Models were constructed using only the data from the participants with complete cognitive data, amounting to 1096 younger (aged 20–37) and 607 older individuals (aged 36–90; because

none of the participants were aged 91–99, the data from 13 participants having a recorded age of 100 were considered as outliers that could interfere with the model fit and were thus excluded). All participants were cognitively normal.

B. Preprocessing

The downloaded T1-weighted images were already pre-processed; only two additional preprocessing steps were thus performed: histogram standardization using the fuzzy c-means algorithm [19] and resampling to $121 \times 145 \times 121$ voxels [5], to reduce memory usage and computation time. Common data augmentation such as scaling, translation, or rotation were not applied due to the MNI registration.

C. Cortical parcellation

As a first test of regional brain age, a relatively coarse cortical parcellation was used, comprising 9 non-overlapping regions per hemisphere: anterior frontal, superior frontal, inferior frontal, central (precentral and postcentral gyrus), parietal (the whole parietal lobe *sans* postcentral gyrus), medial temporal, lateral temporal, occipital, and cingulate. Accordingly, 18 regional brain age models were trained.

D. Architecture of regional brain age models

Our proposed 3D-CNN model combined features from two previous studies [3], [20], and was reported in our previous work [5]. There were five convolution blocks, each containing (1) four alternating convolutional (kernel size = $3 \times 3 \times 3$, stride = 1) and rectified linear unit (ReLU) layers, and (2) a max-pooling layer (kernel size = $2 \times 2 \times 2$, stride = 2) for dimensionality reduction. The number of feature channels is 8, 16, 32, 64, and 128, respectively. The last 3 layers were fully-connected layers designed for regressing the feature vectors onto the output. Deeper architectures were not used to avoid overfitting [21].

E. Model training

The present study was implemented with PyTorch 2.2.2+cu121 in a Python environment (version 3.9.5), with Ubuntu LTS installed on a GPU virtual machine (8-core vCPU, 128GiB vRAM, and 2 RTX-6000 Ada, 48GB GPU Card). Inspired by ensemble methods [9], [22], a technique called nested cross-validation was implemented. Specifically, the whole dataset was split into 10 outer-folds, with each outer-fold involving a development set and a testing set of the ratio 9:1. Under each outer-fold, the development set was further divided into 5 inner-folds, each now having a training set and a validation set of the ratio 4:1. The outer-folds and inner-folds were all split in the presence of stratified sampling to ensure that the age distribution was comparable across folds. While the CNN model was trained using the training set, the validation set was used for evaluating the stopping criterion and for correcting the well-known RttM problem. The final predicted outcome for the testing set was obtained by averaging the prediction outcomes of an ensemble of five models, each associated with one inner-fold. In our previous work on global brain age, this was

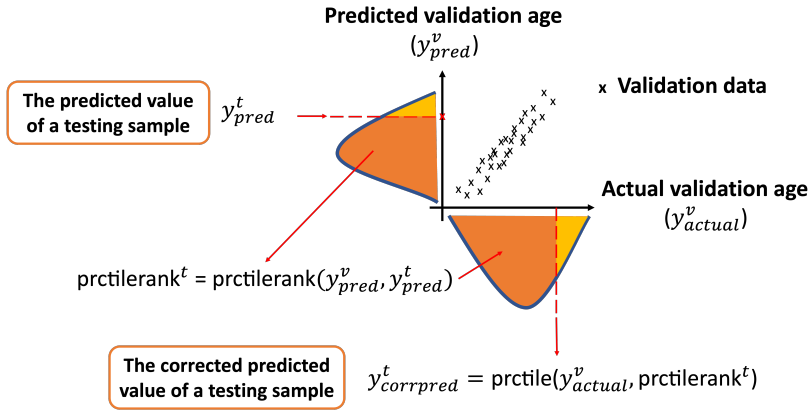


Fig. 1: Illustration of the process of percentile matching.

Algorithm 1: Percentile matching

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1 function prctilematch ( $y_{pred}^v, y_{actual}^v, y_{pred}^t$ );
   Input : Predicted validation ages,  $y_{pred}^v$  (vector)
           Actual validation ages,  $y_{actual}^v$  (vector)
           Predicted testing age,  $y_{pred}^t$  (scalar)
   Output: Corrected predicted testing age,  $y_{corrpred}^t$  (scalar)
2  $prctilerank^t = prctilerank(y_{pred}^v, y_{pred}^t)$ ;
3  $y_{corrpred}^t = prctile(y_{actual}^v, prctilerank^t)$ ;
4 return  $y_{corrpred}^t$ ;

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found to yield better performance [5]. The hyperparameters adopted were as follows: learning rate = 0.0001, batch size = 8, maximum number of epochs = 50 (with early stopping = 8 epochs, i.e., the training of the models was stopped after the validation loss failed to reduce for 8 consecutive epochs). ADAM was used as the optimizer.

F. “Regression to the mean” (RttM) and correction formulae

RttM refers to the overestimation and the underestimation of the predicted values at the two ends of the variable being predicted in a regression problem [16]. Within the context of brain age research, this age-related bias has been corrected using various formulae, e.g., [3], [17], [23], [24], [25]. Typically, these formulae are based on the coefficients of the linear fit between the predicted values (y_{pred}) and the ground truth (y_{actual}):

$$y_{pred} = \alpha \times y_{actual} + \beta \quad (1)$$

from which the actual age that would have corresponded to the resultant predicted regional brain age would be derived. For example, according to Cole’s formula [3], for each testing sample, the corrected predicted value $y_{corrpred}$ is computed as follows:

$$y_{corrpred} = \frac{y_{pred} - \beta}{\alpha} \quad (2)$$

However, as commented by [17], the instability of the denominator in Eq. (2) could introduce undesired variability, leading to extreme values that exceed the actual range of chronological age. The following formula was first proposed by de Lange et al. [26] to correct for this issue:

$$y_{corrpred} = y_{pred} + (y_{actual} - \alpha \times y_{actual} + \beta) \quad (3)$$

However, the inclusion of the actual age in Eq. (3) results in information leakage, thereby yielding favorable metrics (e.g., small MAE) even for poorly performing models [18], [25].

G. Our proposed “percentile matching” method

In view of aforementioned problems with the two formulae, we herewith propose a conceptually simple, non-parametric, and parameter-free method that could achieve

the same purpose as Eq. (1) of linking the predicted brain age with chronological age, based on an idea referred to as “percentile matching”. In brief, for a given test sample, its predicted regional brain age, y_{pred}^t , is corrected using the distributional properties of the validation set (Fig. 1). Let y_{pred}^v and y_{actual}^v be a vector of the predicted regional brain ages and actual chronological age for the validation data, respectively. First, the percentile rank of y_{pred}^t under the distribution of y_{pred}^v would be computed. The corrected predicted regional brain age, $y_{corrpred}^t$, would then be obtained by replacing the original value with the percentile of y_{actual}^v corresponding to this rank. The pseudocode for implementing this method is provided in Fig. 1.

H. Model evaluation

Three factors influencing prediction performance were investigated, including hemisphere (left vs. right), cortical region (9 regions on each hemisphere), and correction for the RttM problem (uncorrected, Cole’s method, de Lange, and percentile matching). The prediction results were evaluated using four metrics: mean absolute error (MAE), root mean square error (RMSE), Spearman’s ρ , and Pearson’s r . Two sets of metrics were computed: (1) to represent the overall prediction performance, the predicted values were concatenated across the 10 outer-folds and compared against the ground truth; (2) to demonstrate the statistical stability across the 10 outer-folds, the mean and standard deviation of these four metrics across outer-folds were also calculated.

III. RESULTS

A. Prediction accuracy for regional brain age models

TABLE I summarizes the overall prediction performance as a function of hemisphere, cortical region, and correction method for the RttM problem, based on concatenating the prediction values across the 10 outer-folds. For each correction method, the optimal performance was highlighted in bold for each hemisphere. For example, for uncorrected result, the best performance on the left hemisphere was achieved at the inferior frontal region for all four metrics (MAE = 4.951 years; RMSE = 6.758 years; Spearman’s

Correction method	Cortical region	Left hemisphere				Right hemisphere			
		MAE	RMSE	ρ	r	MAE	RMSE	ρ	r
Uncorrected	Anterior frontal	5.010	6.957	0.765	0.915	5.773	7.925	0.749	0.882
	Superior frontal	5.415	7.398	0.767	0.898	6.481	8.583	0.764	0.890
	Inferior frontal	4.951	6.758	0.780	0.918	5.585	7.313	0.746	0.903
	Central	6.399	8.547	0.737	0.867	6.397	8.706	0.741	0.858
	Parietal	8.333	11.171	0.693	0.791	6.860	8.979	0.739	0.867
	Medial temporal	5.768	7.892	0.754	0.884	5.584	7.539	0.743	0.895
	Lateral temporal	5.170	6.966	0.759	0.912	5.374	7.222	0.763	0.904
	Occipital	6.035	8.200	0.729	0.874	5.991	8.109	0.733	0.885
	Cingulate	5.019	6.881	0.773	0.913	5.164	7.004	0.755	0.910
Cole	Anterior frontal	5.214	7.182	0.783	0.919	5.779	8.073	0.771	0.901
	Superior frontal	5.269	7.329	0.806	0.917	5.251	7.275	0.806	0.919
	Inferior frontal	5.253	7.111	0.785	0.921	5.111	6.911	0.774	0.924
	Central	5.766	7.997	0.770	0.904	5.674	7.808	0.777	0.907
	Parietal	5.751	7.744	0.772	0.908	5.215	7.013	0.800	0.924
	Medial temporal	5.793	8.022	0.769	0.903	5.817	7.797	0.759	0.909
	Lateral temporal	5.081	6.929	0.784	0.925	4.955	6.844	0.797	0.926
	Occipital	5.632	7.590	0.743	0.912	5.635	7.668	0.750	0.911
	Cingulate	5.434	7.458	0.775	0.914	5.505	7.594	0.765	0.912
Percentile matching	Anterior frontal	4.951	6.884	0.785	0.916	5.473	7.696	0.771	0.894
	Superior frontal	4.974	6.994	0.807	0.913	4.890	6.930	0.809	0.915
	Inferior frontal	4.954	6.706	0.787	0.920	4.911	6.638	0.775	0.921
	Central	5.227	7.364	0.771	0.903	5.275	7.245	0.782	0.906
	Parietal	5.112	7.012	0.773	0.912	4.819	6.638	0.801	0.922
	Medial temporal	5.388	7.570	0.770	0.898	5.385	7.288	0.758	0.906
	Lateral temporal	4.945	6.713	0.785	0.920	4.780	6.586	0.797	0.923
	Occipital	5.479	7.407	0.744	0.912	5.331	7.324	0.750	0.904
	Cingulate	5.182	7.197	0.776	0.908	5.317	7.303	0.765	0.906
de Lange	Anterior frontal	2.255	3.226	0.985	0.995	2.920	3.746	0.968	0.991
	Superior frontal	2.857	3.642	0.962	0.990	4.963	6.217	0.919	0.975
	Inferior frontal	2.200	2.897	0.992	0.998	3.307	4.116	0.953	0.987
	Central	4.911	6.286	0.908	0.969	3.381	4.359	0.944	0.985
	Parietal	6.612	9.307	0.862	0.932	5.245	6.759	0.890	0.960
	Medial temporal	2.672	3.568	0.971	0.992	2.824	3.583	0.975	0.993
	Lateral temporal	2.397	3.266	0.974	0.993	3.062	3.904	0.954	0.986
	Occipital	3.603	4.558	0.939	0.983	3.241	4.453	0.950	0.984
	Cingulate	2.272	2.693	0.993	0.998	2.259	2.915	0.991	0.996

TABLE I: Overall prediction performances of regional brain age models by hemisphere, region, and correction method.

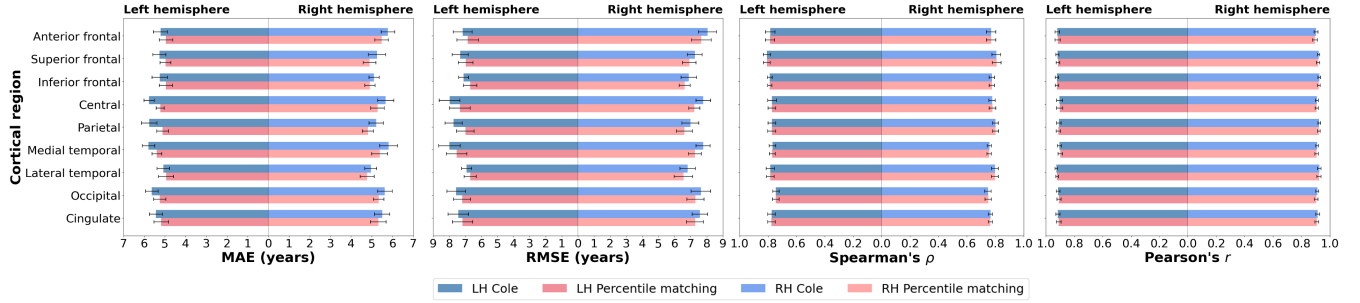


Fig. 2: The mean evaluation metrics taken across the 10 outer-folds, for Cole’s method and the percentile matching method. The error bars represent the standard deviation.

$\rho = 0.780$; and Pearson’s $r = 0.918$). Relative to the uncorrected results, the three correction methods resulted in an improved (i.e., smaller) MAE—the most often used metric in the literature—for 11 of 18 (Cole), 15 of 18 (percentile matching), and 18 of 18 (de Lange) cases, respectively. Between these three methods, although numerically the best metric was almost always attained for de Lange’s method, this does not necessarily imply a better prediction performance of cognitive functions [9] (see Section III-C).

To statistically compare the methods, the summary statistics (mean and standard deviation) of each metric were computed across the 10 outer-folds, for all correction methods (they are openly available at <https://osf.io/>

[a962y/](https://osf.io/)). The comparisons between Cole and percentile matching are visualized in Fig. 2, where it is clear that the latter method yielded significantly smaller mean MAE and mean RMSE for all 18 of 18 regions. For the two correlation metrics, the pattern was subtler, with the percentile matching method yielding a significantly larger mean Spearman’s ρ for 14 of 18 regions, $t(17) = 2.50$, $p = 0.014$, but a significantly smaller mean Pearson’s r for 17 of 18 regions, $t(16) = -5.41$, $p < .001$. This pattern was observed because unlike Spearman’s ρ which depends only on the rank-order, Pearson’s r is more easily inflated by the presence of outlying corrected predicted ages for Cole’s method.

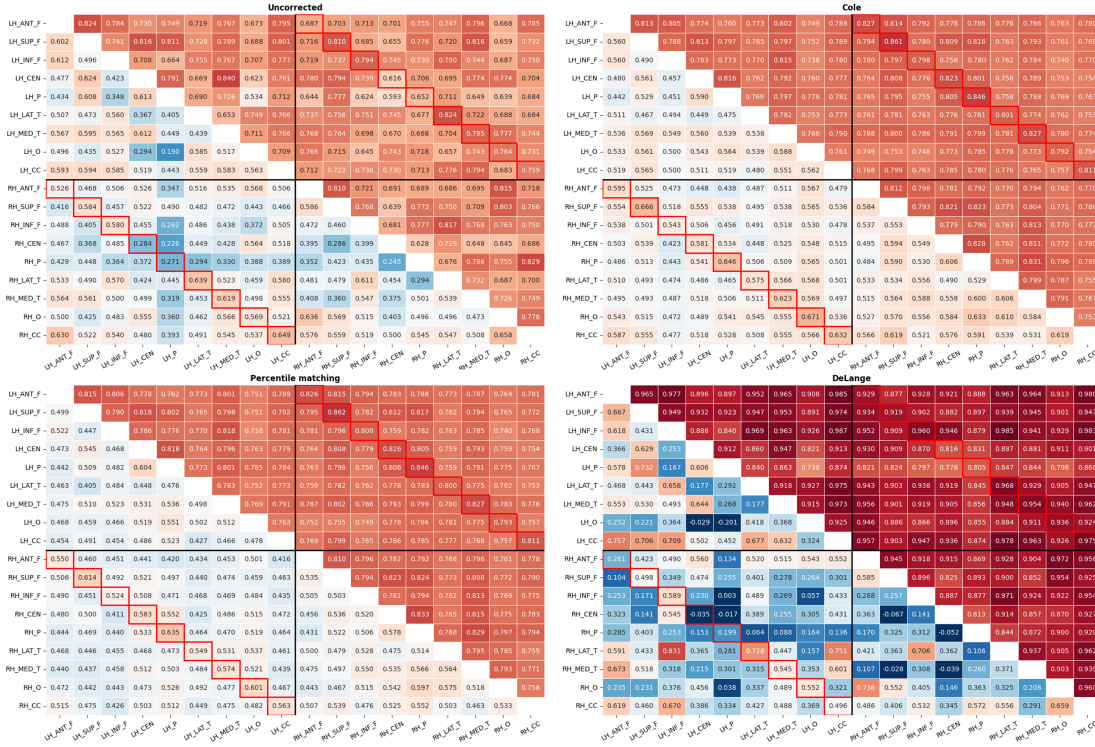


Fig. 3: Correlation matrices for the predicted regional brain ages (upper right triangle) and the corresponding brain age gaps (lower left triangle), for each correction method. The cells for homotopic correlations were encircled in red.

B. Symmetry properties of regional brain age measures

Under the assumption that homotopic regions are driven by a similar process of ageing, the correlations of regional brain age between homotopic regions were expected to be larger than those between non-homotopic regions. Fig. 3 illustrates this point through the correlation matrices for both predicted regional brain ages (upper right triangle) and the corresponding predicted brain age gaps (lower left triangle). The cells for homotopic correlations were encircled in red. It is worth noting that only for Cole’s method and for the percentile matching method could we observe a clear trend that the homotopic correlations on the regional brain age gaps were stronger than their non-homotopic counterparts (TABLE II). Specifically, the homotopic correlations were stronger than 100% (16 out of 16) of the across-hemispheric correlations for both Cole’s and the percentile matching method. In terms of within-hemispheric correlation, the percentile matching method was better, achieving a minimum of 87.5% compared to the 56.25% for Cole’s method. In contrast, such consistency was observed for neither the uncorrected method nor the de Lange’s method. In fact, as will be shown below, the de Lange’s method would result in the worst correlation with cognitive functions. Similar finding was also observed for regional brain age (not shown).

C. Associations with fluid and crystallized intelligence

TABLE III summarizes the Spearman’s correlations between regional brain age measures with the two intelligence measures. Given that both intelligence measures are nega-

tively associated with the chronological age and that the predicted regional brain age was strongly associated with the chronological age (TABLE I), it was not surprising that there were significant negative associations between the predicted regional brain age and both intelligence measures for all cases examined. In fact, regardless of the correction method used, the Spearman’s correlation always ranged from -0.20 to -0.28 for crystallized intelligence, and from -0.45 to -0.55 for fluid intelligence. What needs to be tested was whether there remains direct correlation between regional brain age and the intelligence measures after the chronological age was factored out. As such, Spearman’s partial correlations were computed. Our results showed clearly that, with the exception of the de Lange’s method, the partial correlations remain significant for all cases examined, including those obtained using the uncorrected regional brain age measures. From this point of view, despite achieving the small MAE, de Lange’s method yielded regional brain age measures that were the worst in predicting intelligence, with the associations being entirely driven by chronological age.

IV. DISCUSSION

In the present study, regional brain age models were constructed using convolutional neural networks for a coarse parcellation of 9 cortical regions per hemisphere. Apart from characterizing the resultant regional brain age measures using conventional metrics (e.g., MAE), we evaluated these measures from two novel aspects: (1) their symmetry properties, and (2) the extent of associations with crystallized

Correction	Cortical region	Homotopic	Within (%)	Across (%)
Uncorrected	Anterior frontal	0.526	56.25	62.50
	Superior frontal	0.584	62.50	100.00
	Inferior frontal	0.580	81.25	100.00
	Central	0.284	6.25	6.25
	Parietal	0.271	12.50	12.50
	Medial temporal	0.639	100.00	100.00
	Lateral temporal	0.619	100.00	100.00
	Occipital	0.569	81.25	100.00
	Cingulate	0.649	93.75	100.00
Cole	Anterior frontal	0.595	100.00	100.00
	Superior frontal	0.666	100.00	100.00
	Inferior frontal	0.543	56.25	100.00
	Central	0.581	75.00	100.00
	Parietal	0.646	100.00	100.00
	Medial temporal	0.575	87.50	100.00
	Lateral temporal	0.623	100.00	100.00
	Occipital	0.671	100.00	100.00
	Cingulate	0.632	100.00	100.00
Percentile matching	Anterior frontal	0.550	100.00	100.00
	Superior frontal	0.614	100.00	100.00
	Inferior frontal	0.524	87.50	100.00
	Central	0.583	93.75	100.00
	Parietal	0.635	100.00	100.00
	Medial temporal	0.549	87.50	100.00
	Lateral temporal	0.574	100.00	100.00
	Occipital	0.601	100.00	100.00
	Cingulate	0.563	100.00	100.00
de Lange	Anterior frontal	0.261	18.75	25.00
	Superior frontal	0.498	56.25	93.75
	Inferior frontal	0.589	75.00	87.50
	Central	-0.035	18.75	0.00
	Parietal	0.199	31.25	56.25
	Medial temporal	0.728	100.00	87.50
	Lateral temporal	0.545	81.25	87.50
	Occipital	0.552	87.50	100.00
	Cingulate	0.496	37.50	68.75

TABLE II: The homotopic associations between regional brain age gaps and the percentage of non-homotopic associations (within- or across-hemispheric) that were smaller in strength relative to the corresponding homotopic pair.

and fluid intelligence. Beyond this primary focus, we also compared different ways of correcting for the “regression to the mean” (RttM) problem. Regarding (1), our results confirmed the expectation that homotopic region-pairs (e.g., between left and right occipital lobes) would tend to age similarly, thereby having stronger associations on regional brain age gap compared to their non-homotopic counterparts (divided into within- and across-hemispheric pairs). Such findings were most robustly observed with the Cole’s method and the percentile matching method we proposed for correction. Regarding (2), we showed that the regional brain age measures were directly associated with both crystallized and fluid intelligence, having significant partial correlations with the intelligence measures after factoring out the influence of the chronological age. This finding could be robustly observed with the exception of the measures corrected by de Lange’s method. These findings underline the promise of the regional brain age measures in predicting intelligence and by extrapolation, more specific cognitive functions.

Regarding the choice of the correction method, we concluded that only Cole’s and the percentile matching method could result in regional brain age measures that have the desirable properties, specifically the symmetry properties

and the direct associations with intelligence measures. Between these two methods, the percentile matching method consistently outperformed the Cole’s method in terms of MAE, RMSE, and Spearman’s correlation, although which method provided the optimal correction should be further validated with other datasets. By comparison, although de Lange’s method yielded the best evaluation metrics, the method runs the risk of information leakage [18], [25] and could not display the desirable symmetry and association properties, and should thus be avoided in future studies. A main limitation of the present study is that we only developed regional brain age models for the cerebral cortex but not yet for subcortical regions like the basal ganglia and cerebellum. However, the same general pipeline used in the present study can be used for this purpose. Future studies will fill this gap to determine whether the regional brain age for sub-cortical regions showed similar symmetry and association properties.

V. CONCLUSIONS

We successfully characterized the symmetry properties of regional brain age measures and revealed the direct associations between regional brain age measures and both crystallized and fluid intelligence.

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DATA AVAILABILITY STATEMENT

This research study was conducted using the data downloaded from the Human Connectome Project (www.humanconnectome.org, including the restricted access of demographic info) and the National Institute of Mental Health Data Archive under an approved Data Use Certification. Per the user licence, ethics approval was not required.

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Correction	Cortical region	Crystallized intelligence								Fluid intelligence							
		Correlation				Partial correlation				Correlation				Partial correlation			
		LH		RH		LH		RH		LH		RH		LH		RH	
		ρ	pval	ρ	pval	ρ	pval	ρ	pval	ρ	pval	ρ	pval	ρ	pval	ρ	pval
Uncorrected	Anterior frontal	-0.259	0.000	-0.267	0.000	-0.151	0.000	-0.166	0.000	-0.488	0.000	-0.495	0.000	-0.126	0.000	-0.151	0.000
	Superior frontal	-0.238	0.000	-0.253	0.000	-0.118	0.000	-0.143	0.000	-0.486	0.000	-0.493	0.000	-0.121	0.000	-0.136	0.000
	Inferior frontal	-0.254	0.000	-0.257	0.000	-0.142	0.000	-0.150	0.000	-0.511	0.000	-0.494	0.000	-0.157	0.000	-0.152	0.000
	Central	-0.241	0.000	-0.245	0.000	-0.127	0.000	-0.132	0.000	-0.473	0.000	-0.465	0.000	-0.120	0.000	-0.104	0.000
	Parietal	-0.223	0.000	-0.234	0.000	-0.107	0.000	-0.116	0.000	-0.457	0.000	-0.488	0.000	-0.127	0.000	-0.146	0.000
	Medial temporal	-0.251	0.000	-0.269	0.000	-0.140	0.000	-0.168	0.000	-0.495	0.000	-0.491	0.000	-0.148	0.000	-0.149	0.000
	Lateral temporal	-0.264	0.000	-0.227	0.000	-0.161	0.000	-0.102	0.000	-0.490	0.000	-0.467	0.000	-0.134	0.000	-0.089	0.000
	Occipital	-0.233	0.000	-0.270	0.000	-0.115	0.000	-0.171	0.000	-0.468	0.000	-0.492	0.000	-0.118	0.000	-0.158	0.000
	Cingulate	-0.257	0.000	-0.271	0.000	-0.149	0.000	-0.171	0.000	-0.492	0.000	-0.499	0.000	-0.128	0.000	-0.154	0.000
Cole	Anterior frontal	-0.273	0.000	-0.264	0.000	-0.174	0.000	-0.160	0.000	-0.505	0.000	-0.493	0.000	-0.145	0.000	-0.132	0.000
	Superior frontal	-0.246	0.000	-0.245	0.000	-0.128	0.000	-0.126	0.000	-0.502	0.000	-0.488	0.000	-0.119	0.000	-0.091	0.000
	Inferior frontal	-0.249	0.000	-0.256	0.000	-0.134	0.000	-0.147	0.000	-0.508	0.000	-0.503	0.000	-0.149	0.000	-0.147	0.000
	Central	-0.227	0.000	-0.254	0.000	-0.100	0.000	-0.143	0.000	-0.468	0.000	-0.492	0.000	-0.085	0.000	-0.125	0.000
	Parietal	-0.220	0.000	-0.253	0.000	-0.090	0.000	-0.140	0.000	-0.481	0.000	-0.505	0.000	-0.108	0.000	-0.131	0.000
	Medial temporal	-0.252	0.000	-0.262	0.000	-0.141	0.000	-0.158	0.000	-0.498	0.000	-0.489	0.000	-0.142	0.000	-0.133	0.000
	Lateral temporal	-0.270	0.000	-0.244	0.000	-0.170	0.000	-0.126	0.000	-0.503	0.000	-0.499	0.000	-0.139	0.000	-0.123	0.000
	Occipital	-0.261	0.000	-0.272	0.000	-0.156	0.000	-0.174	0.000	-0.495	0.000	-0.510	0.000	-0.157	0.000	-0.178	0.000
	Cingulate	-0.264	0.000	-0.276	0.000	-0.159	0.000	-0.179	0.000	-0.498	0.000	-0.499	0.000	-0.138	0.000	-0.146	0.000
Percentile matching	Anterior frontal	-0.273	0.000	-0.264	0.000	-0.174	0.000	-0.161	0.000	-0.506	0.000	-0.494	0.000	-0.145	0.000	-0.133	0.000
	Superior frontal	-0.248	0.000	-0.250	0.000	-0.131	0.000	-0.135	0.000	-0.502	0.000	-0.493	0.000	-0.120	0.000	-0.101	0.000
	Inferior frontal	-0.247	0.000	-0.257	0.000	-0.131	0.000	-0.149	0.000	-0.510	0.000	-0.505	0.000	-0.151	0.000	-0.151	0.000
	Central	-0.228	0.000	-0.257	0.000	-0.102	0.000	-0.148	0.000	-0.472	0.000	-0.497	0.000	-0.091	0.000	-0.130	0.000
	Parietal	-0.224	0.000	-0.251	0.000	-0.094	0.000	-0.137	0.000	-0.483	0.000	-0.504	0.000	-0.112	0.000	-0.128	0.000
	Medial temporal	-0.251	0.000	-0.261	0.000	-0.140	0.000	-0.156	0.000	-0.497	0.000	-0.489	0.000	-0.139	0.000	-0.134	0.000
	Lateral temporal	-0.269	0.000	-0.244	0.000	-0.168	0.000	-0.125	0.000	-0.503	0.000	-0.497	0.000	-0.140	0.000	-0.117	0.000
	Occipital	-0.265	0.000	-0.272	0.000	-0.162	0.000	-0.173	0.000	-0.499	0.000	-0.510	0.000	-0.162	0.000	-0.177	0.000
	Cingulate	-0.263	0.000	-0.279	0.000	-0.158	0.000	-0.184	0.000	-0.498	0.000	-0.500	0.000	-0.136	0.000	-0.149	0.000
de Lange	Anterior frontal	-0.224	0.000	-0.211	0.000	-0.084	0.001	-0.020	0.416	-0.551	0.000	-0.533	0.000	-0.069	0.005	-0.006	0.800
	Superior frontal	-0.222	0.000	-0.203	0.000	-0.061	0.012	-0.019	0.445	-0.538	0.000	-0.509	0.000	-0.040	0.095	-0.015	0.550
	Inferior frontal	-0.212	0.000	-0.211	0.000	-0.005	0.843	-0.024	0.319	-0.548	0.000	-0.535	0.000	-0.028	0.255	-0.047	0.053
	Central	-0.208	0.000	-0.216	0.000	-0.035	0.150	-0.044	0.067	-0.513	0.000	-0.540	0.000	-0.042	0.084	-0.079	0.001
	Parietal	-0.213	0.000	-0.223	0.000	-0.059	0.015	-0.075	0.002	-0.509	0.000	-0.514	0.000	-0.083	0.001	-0.067	0.005
	Medial temporal	-0.219	0.000	-0.210	0.000	-0.050	0.037	-0.008	0.737	-0.544	0.000	-0.539	0.000	-0.054	0.026	-0.017	0.492
	Lateral temporal	-0.214	0.000	-0.228	0.000	-0.027	0.270	-0.081	0.001	-0.542	0.000	-0.548	0.000	-0.036	0.142	-0.097	0.000
	Occipital	-0.228	0.000	-0.213	0.000	-0.081	0.001	-0.033	0.178	-0.538	0.000	-0.529	0.000	-0.080	0.001	-0.029	0.228
	Cingulate	-0.218	0.000	-0.217	0.000	-0.049	0.042	-0.042	0.080	-0.550	0.000	-0.546	0.000	-0.045	0.064	-0.021	0.381

TABLE III: Correlation and partial correlation between regional brain age measures and crystallized and fluid intelligence. The partial correlation was calculated with the chronological age factored out.

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