MRI-informed brain age matrices as potential personalized biomarkers for ageing brain

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ABSTRACT

The prevalence of neurodegenerative diseases is increasing as the population ages, imposing significant burdens on society and individuals. The World Health Organization (WHO) has estimated that approximately 5% of the global older population which amounts to around 82 million people, will suffer from age-related neurodegenerative disorders. Consequently, there is a growing trend toward establishing biomarkers that can quantify an individual's brain health and provide risk assessments for age-associated neurodegenerative disorders at the single-subjects level. One promising neuroimaging-derived biomarker, known as 'brain age matrices', including 'brain age' and 'brain-PAD', has been explored to predict individual brain aging trajectories, identify cognitive function deterioration, and aid in the early detection of certain neurodegenerative diseases.

Support vector machine (SVM) is performed to capture the multidimensional aging patterns across the whole brain, with the regional-/voxel-wise features from the structure MRI as the input variables. Subsequently, 'brain age' can be estimated individually. The difference between the predicted brain age and chronological age is defined as 'brain-PAD'. The 'brain-PAD' (brain-predicted age difference) is employed to quantify the deviations of an individual's brain ageing from the healthy brain ageing progress. A positive score of 'brain-PAD' indicates accelerated brain ageing, while a negative score suggests delayed brain ageing or maturation.

Our research team has examined the brain age matrices in healthy ageing population, individuals with mild neurocognitive disorders, and patients with neurodegenerative diseases. We discovered that the score of 'brain-PAD' is +10 years in Alzheimer's disease (AD) and +6.2 years in patients with mild cognitive impairment (MCI). Furthermore, through component-specific decoding of verbal fluency performance, we found a significant correlation between higher brain age matrices and worse global cognitive function and executive function in mild neurocognitive disorder (NCD) patients compared to healthy aging subjects. However, several research challenges remain. These include expanding the application of brain age matrices in clinical contexts, enhancing the accuracy of brain age prediction models, and simulating further investigation into the prognosis of specific clinical interventions for age-related neurodegenerative diseases.

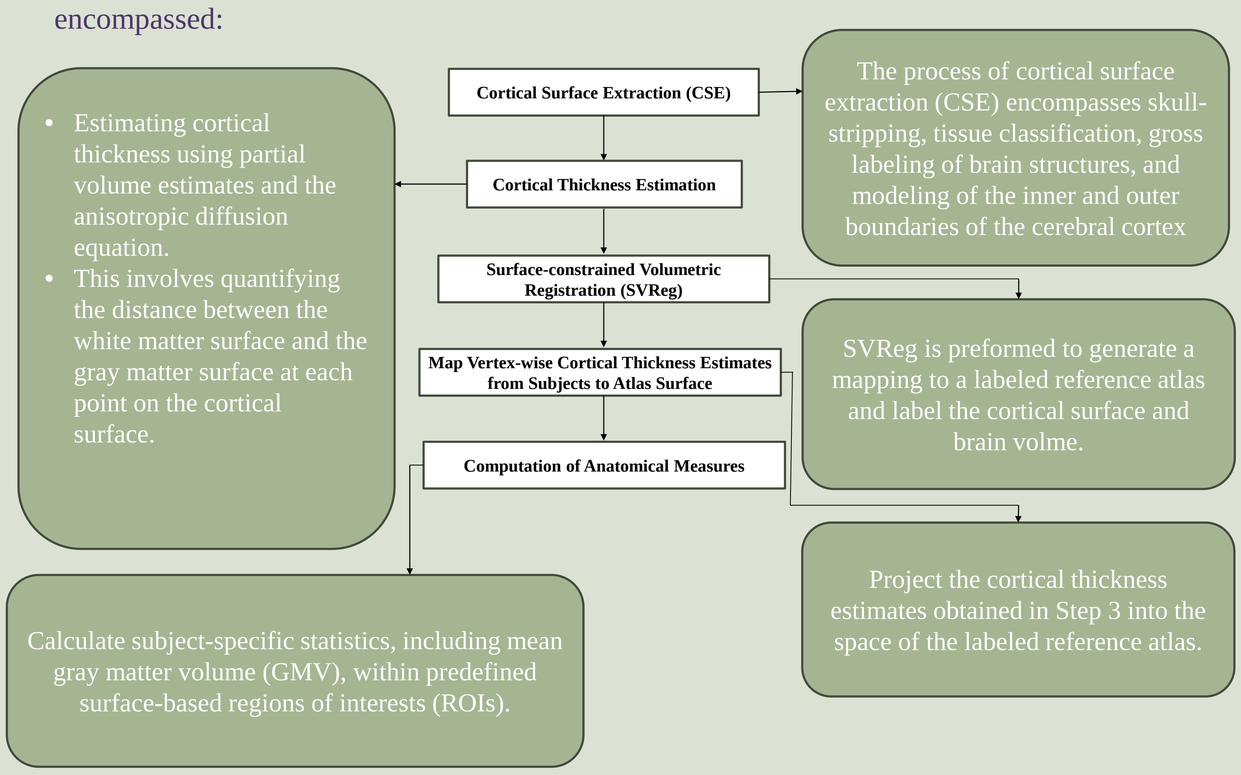
MATERIALS

The training sample is the T1 weighted MRI scans of adult brains sourced from a publicly accessible datasets: the Cambridge Centre for Aging and Neuroscience (Cam-CAN) dataset (https://www.cam-can.org/index.php?content=dataset) (N=611, age range: 18-90).

The testing samples are the community-dwelling right-handed old adults aged from 65 to 85 years recruited from our previous cohort studies. There are two clinical sub-samples in the testing set: normal ageing elderly and the mild NCD patients. The demographic were comparable between normal ageing elderly and mild NCD patients.

Clinical features	Normal ageing ($n = 36$)	Mild NCD ($n = 16$)	t Value (χ^2)	p Value
Age	70.54 ± 3.65	72.04 ± 4.62	−1.253	0.216
Sex (F/M)	23/13	10/6	2.002	0.059
Education (years)	8.83 ± 4.81	8.72 ± 3.04	0.087	0.931
CSDD	0.28 ± 1.11	0.38 ± 0.89	−0.309	0.759
PSQI	5.33 ± 3.58	5.38 ± 4.27	−0.036	0.971
ADL	0.99 ± 0.01	0.98 ± 0.04	2.082	0.042
CDR-SOB	0.25 ± 0.41	0.59 ± 0.45	−2.718	0.009
CMMSE	28.31 ± 1.28	27.51 ± 1.55	1.959	0.056
HK MoCA	27.61 ± 1.55	25.19 ± 2.26	4.495	<0.001
DSF	7.69 ± 0.89	7.06 ± 1.56	1.851	0.071
DSB	3.69 ± 1.35	2.94 ± 0.68	2.121	0.039
TMT-A	12.49 ± 6.47	15.25 ± 7.18	−1.375	0.175
TMT-B	67.27 ± 46.73	83.16 ± 41.91	−1.166	0.249
Brain age	68.11 ± 6.62	77.91 ± 7.13	−4.811	<0.001
BrainAGE	−2.43 ± 5.21	5.86 ± 4.07	−6.202	<0.001

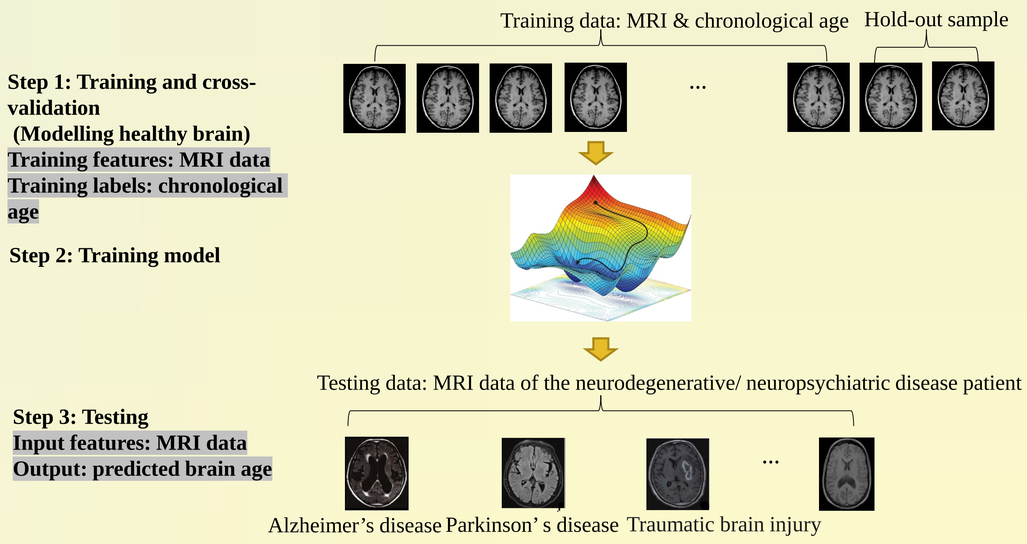
All T1-weighted MRI scans are pre-processed with cortical reconstructions and surface-based morphometry (SBM) analyses using BrainSuite 21a software (https://brainsuite.org/). BrainSuite is a comprehensive automatic cortical surface identification package extensively employed in dementia and aging research. The key stages of the preprocessing pipeline encompassed:



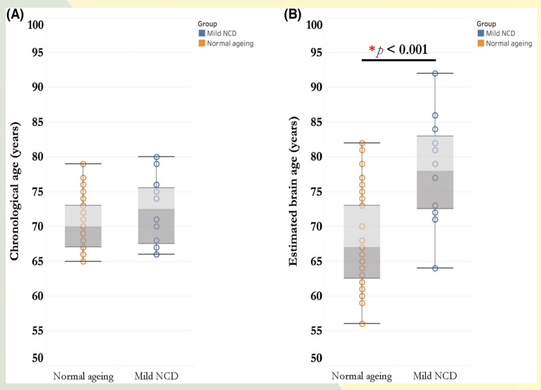
METHODS

To get the individual 'brain-PAD', there are four steps:

- The first step is training and validating the brain age prediction model by modelling neuroimaging data from healthy subjects (Cam-CAN). The training features are the pre-processed neuroimaging data, and the training labels are the chronological age of these subjects. In our study, the T1-weighted MRI scans are pre-processed into regional GMV, GMT, WMV and CSF volumes.
- The second step is the training of the brain age prediction model utilizing the support vector regression model (SVR).
- Thirdly, in the testing step, with the neuroimaging data of independent patients as input features, the predicted brain age could be calculated with the well-established brain-age prediction framework. After the three steps, the predicted brain age aggregates the multidimensional aging pattern across the whole brain into a single value just with the individual's MRI data.
- Finally, The 'brain-PAD' is the difference between the predicted brain age and the individual's chronological age. For 'brain-PAD', the positive value indicates the accelerating brain ageing, whereas negative value indicates delayed brain maturation/ageing process. The individual 'brain-PAD' can directly quantify the amount of acceleration or deceleration of brain ageing process.



RESULTS

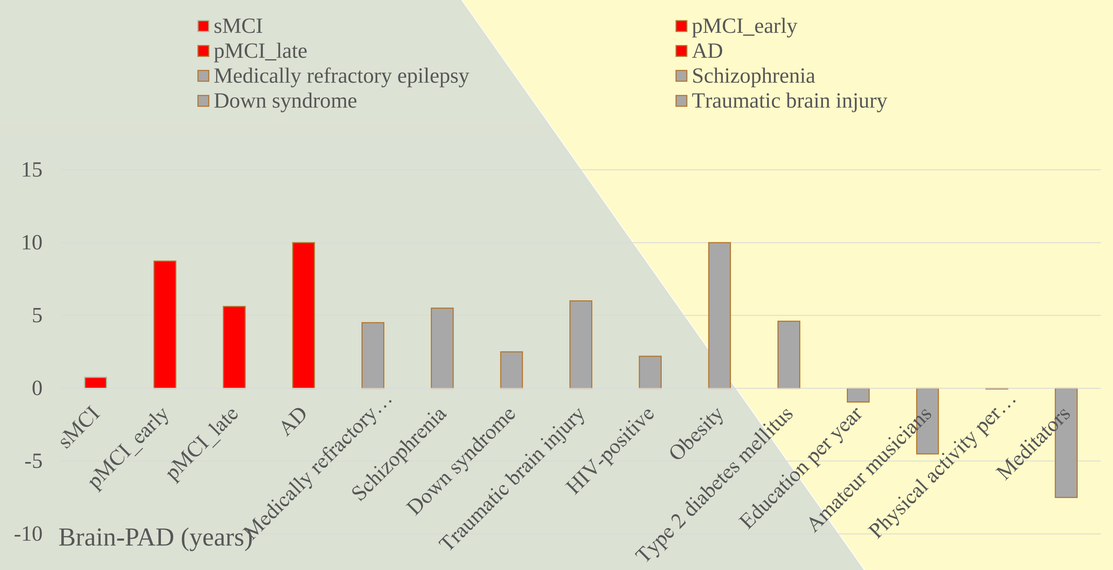


Comparisons of chronological age and estimated brain age in normal ageing elderly and mild neurocognitive disorder (NCD) patients.

(A) There was no difference of chronological age between normal ageing elderly and mild NCD patients.

(B) Mild NCD patients had older brain age than chronological age-matched normal ageing elderly.

OTHER CLINICAL APPLICATIONS



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