Initial exploration of a brain age score based on validated computerized cognitive assessments in Japanese individuals

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This analysis was based on screening data from the MissionAD (elenbecestat) Phase 3 studies. The MissionAD studies were conducted by Eisai Co Ltd.

Background

Cognitive and/or neuropsychological tests typically have abstract outcome measures, where the clinical meaning of scores is not readily apparent. For clinicians, this is commonly achieved through an understanding of the normal distribution of scores, for example bone density t-scores in evaluating osteoporosis. This may not be well understood by patients and study participants though, and here the concept of being 'normal for one's age' may also be valuable. A difference between chronological age and biological age has been used to more easily communicate health related information. Our team aimed to develop a 'Brain Age' score for communicating cognitive test performance.

Methods

In our study, Brain Age was derived as the difference in standardized score on a computerized cognitive assessment from age matched normative data. We used the Cogstate Learning and Working Memory composite, which requires scores on the One Card Learning and One Back tests, administered as part of the Cogstate Brief Battery.

Our Brain Age score starts with the participants' chronological age and then adjusts based on composite test performance, to give a Brain Age up to 10 years younger or older. For every point better or worse than the norm, 0.5 years was added or subtracted from chronological age.

Learning and Working Memory composite from the Cogstate Brief Battery and Cognigram™ demonstrates…

Large impairments in MCI (g = 2.2) and AD (g = 3.3)	High test-retest reliability (r = 0.95)	High classification accuracy (AUC = 0.91 for MCI / 0.99 for AD)

Data were analysed from a subset of Japanese individuals who had been involved in two key clinical trials: 106 cognitively normal individuals from a Japanese normative data sample, and 611 individuals screened for the Eisai elenbecestat MissionAD program who were cognitively impaired on a word list learning test. Mean chronological age was similar in the samples, at around 72 years old (Cognitively normal: 71.7 (SD 4.55); MissionAD: 72.6 (SD 7.41).

Cognitively Normal	Cognitively Impaired (Eisai MissionAD Program)	Average Age (Similar between samples)	Analyzed:
106 individuals	611 individuals	72 Cognitively Normal: 71.7 (SD 4.55) MissionAD: 72.6 (SD 7.41)	Construct validity, known groups validity and test-retest reliability

Results

We evaluated construct validity, known groups validity and test-retest reliability of the brain age score.

- Test completion rates were high, at greater that 99%, supporting acceptability of the tests.
- Brain Age score was higher in clinically impaired individuals versus cognitively normal individuals. Against the background chronological age of around 72, the Brain Age for impaired individuals was 78.9 (SD 8.15) years and for cognitively normal individuals it was 72.4 years (SD 7.45), with a Cohen's d effect size difference of 0.81.
- The intraclass correlation coefficient (ICC) for test-retest was 0.85, indicating high reliability.

Acceptability
Test completion rates high (>99%)

Known Groups Validity
Clinically impaired brain age = 78.9
Cognitively normal brain age = 72.4
(Cohen's d = 0.81)

Test-Retest Reliability
Screening visit 1 to 3 in cognitively normal, ICC = 0.85, indicating high reliability

Conclusions

This initial study suggests a Brain Age score based on the Learning and Working Memory composite from the Cogstate Brief Battery is an acceptable and reliable measure for repeated assessment in Japanese individuals.

Data show Brain Age score as substantially increased versus chronological age in individuals with poorer memory performance on a word list learning test. Further analyses are planned to confirm these properties in other languages and cultures.

In short, the Brain Age score may be a useful means of communicating brain health information, including the need to adopt a healthier lifestyle.

Brain Age may also provide a means by which patient and caregiver insights on meaningful change and difference in scores as a result of disease progression and treatment intervention can be established.

Brain Age score based on the LWM composite of the CBB is an acceptable and reliable measure for repeated assessment in Japanese individuals. Brain Age score increased versus chronological age in individuals with poorer memory performance on a word list learning test.

The Brain Age score may be a useful means of communicating brain health information, including the need to adopt a healthier lifestyle.

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