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Oita University
Eisai Co., Ltd.

DEVELOPMENT OF PREDICTION MODEL FOR BRAIN AMYLOID-BETA ACCUMULATION FOR EARLY SCREENING OF ALZHEIMER'S DISEASE

MACHINE LEARNING MODEL USING DATA THAT CAN BE COLLECTED IN DAILY MEDICAL EXAMINATIONS BY PRIMARY CARE PHYSICIANS

Oita University and Eisai Co., Ltd. (Eisai) announced today the development of a machine learning model to predict amyloid beta*1 (Aβ) accumulation in the brain, combining background data such as age, gender, smoking history and medical history, as well as general blood test and MMSE*2 items. This model is expected to enable primary care physicians to predict the accumulation of brain Aβ, which is an important pathological factor of Alzheimer's disease*3 (AD), during routine medical examinations and to facilitate simple early screening for AD.
The details of this model were published in the online edition of the peer-reviewed medical journal *Alzheimer's Research & Therapy* on January 21, 2025.

Currently, although brain Aβ accumulation can be detected by positron emission tomography*4 (amyloid PET) and cerebrospinal fluid testing*5 (CSF testing), the high cost and invasiveness of these tests are recognized as issues. Therefore, in recent years, numerous studies have been conducted on various AD-related blood biomarkers as a more convenient screening method. However, there is almost no research evaluating the predictive performance of models for brain Aβ accumulation using routine clinical data. This study is the first to develop a machine learning model for prediction of amyloid PET positivity using 34 clinical data items consisting of background data (such as age, gender, smoking history, and medical history), general blood test data (such as kidney function, liver function, and thyroid function), and MMSE items, which are routinely collected in dementia care. The evaluation metric of the prediction model, the Area Under the Curve (AUC), was 0.70 for the model combining background data and general blood test data, and 0.73 for the model combining background data, general blood test data, and MMSE data, indicating a certain level of predictive accuracy.

Anti-Aβ antibody has been shown to potentially provide greater benefit when treatment is initiated at an earlier stage of AD[1] , making early detection of Aβ accumulation in the brain crucial. This machine learning model can predict brain Aβ accumulation using clinical data that can be collected during routine medical care, and so is expected to be widely used by primary care physicians for early screening of AD.
By utilizing the model to determine the necessity of amyloid PET and CSF tests, it is anticipated to lead to early diagnosis and treatment initiation for AD, as well as a reduction in the economic and physical burden on patients.

【Glossary of Terms】

*1 Amyloid beta: A protein viewed as a cause of Alzheimer's disease, which accumulates in the brain for about 20 years prior to the onset of the disease and forms senile plaques

*2 MMSE (Mini-Mental State Examination): A method for evaluating cognitive function. It consists of evaluation items such as orientation, memory, attention/calculation, delayed recall, naming, repetition, comprehension, reading, writing, and figure copying, and is evaluated between 30 to 0 points (normal to severe).

*3 Alzheimer's disease: the most common cause of dementia, and its pathological characteristics include senile plaques, neurofibrillary tangles, and neuronal cell death

*4 Amyloid PET: a brain imaging test visualizing Aβ accumulation in the brain

*5 Cerebrospinal fluid testing: A test analyzing cerebrospinal fluid for Aβ42, phosphorylated tau, and total tau as biomarkers of Alzheimer's disease

Background and Outline of Research

As Japan has become a super-aging society with the rise in the number of dementia patients over the age of 65, the development of new therapeutic agents for AD, the most common cause of dementia, is an urgent issue. In AD, accumulation of Aβ in the brain is a pathological event that precedes onset. It has been shown that anti-Aβ antibody could offer greater benefit if treatment is initiated at earlier stages of AD[1], highlighting the importance of earlier detection of Aβ accumulation in the brain. While imaging such as amyloid PET useful for AD diagnosis and fluid biomarkers are used for detection, these methods have challenges related to invasiveness and cost.

Therefore, many machine learning-based brain Aβ prediction models have been developed as simpler screening tools, but often these models incorporate markers not measured in routine clinical practice, such as imaging data and ApoE genotype. This study is the first to attempt the development of a machine learning model to predict amyloid PET positivity using only background data and general blood test results routinely collected in dementia care.

Results and Significance of Research

This research utilized outpatient data from Oita University Hospital collected between September 2012 and November 2017, and data from a prospective cohort study (USUKI STUDY) on the elderly without dementia aged 65 and older living in Usuki City, Oita Prefecture, conducted between October 2015 and November 2017. The prediction model was created using three machine learning techniques: Support Vector Machine, Elastic Net, and L2 regularization logistic regression, combining 12 items on participants' backgrounds (age, gender, smoking history, medical history - hypertension, dyslipidemia, heart disease, stroke, diabetes, thyroid disease), 11 general blood test items (kidney function, liver function, thyroid function, etc.), and 11 MMSE item scores of 262 individuals (136 men, 126 women, median age 73.8 years) with mild cognitive impairment or normal cognitive function, and evaluating the model’s performance.

For the prediction performance using L2 regularization logistic regression, both the model combining participant backgrounds and MMSE items and the model combining participant backgrounds and general blood tests showed an AUC of 0.70, indicating similar performance. Furthermore, the model that combined all of these elements (participant backgrounds, general blood tests, and MMSE items) showed an improved performance with an AUC of 0.73. Analyzing the key factors contributing to the prediction of Aβ

accumulation identified delayed recall and place orientation among MMSE items, age, thyroid-stimulating hormone, and mean corpuscular volume as important factors.

Academic Paper:

Title: Machine learning models for dementia screening to classify brain amyloid positivity on positron emission tomography using blood markers and demographic characteristics: a retrospective observational study

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