CURRENT OPINION

Machine learning, artificial intelligence and the prediction of dementia

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Purpose of review
Artificial intelligence and its division machine learning are emerging technologies that are increasingly applied in medicine. Artificial intelligence facilitates automatization of analytical modelling and contributes to prediction, diagnostics and treatment of diseases. This article presents an overview of the application of artificial intelligence in dementia research.

Recent findings
Machine learning and its branch Deep Learning are widely used in research to support in diagnosis and prediction of dementia. Deep Learning models in certain tasks often result in better accuracy of detection and prediction of dementia than traditional machine learning methods, but they are more costly in terms of run times and hardware requirements. Both machine learning and Deep Learning models have their own strengths and limitations. Currently, there are few datasets with limited data available to train machine learning models. There are very few commercial applications of machine learning in medical practice to date, mostly represented by mobile applications, which include questionnaires and psychometric assessments with limited machine learning data processing.

Summary
Application of machine learning technologies in detection and prediction of dementia may provide an advantage to psychiatry and neurology by promoting a better understanding of the nature of the disease and more accurate evidence-based processes that are reproducible and standardized.

Keywords
artificial intelligence, cognitive impairment, dementia, machine learning

INTRODUCTION

Mental disorders are a leading cause of health loss and disability worldwide, accounting for the largest proportion of disability-adjusted life-years (DALYs) (56.7%) after neurological disorders (28.6%) [1]. Dementia is a disease at the junction of mental and neurological conditions, and a major global health concern amongst the growing aged population worldwide. According to the WHO (2019), the prevalence and burden of dementia has increased worldwide with about 10 million new cases reported each year, and this number is projected to triple by 2050. Therefore, dementia has been identified by the WHO as a priority for public health and social assistance worldwide [2].

Although there has been extensive research on human biological markers for mental health conditions including dementia, there is lack of reliable laboratory tests and objective technical tools for accurate prediction of dementia in clinical practice, and clinicians mostly rely on evaluation of cognitive functions, psychometric tests and medical history. This potentially leads to subjectivity and human bias of medical assessments affecting both diagnosis and treatment. Therefore, there is a need for diagnostic and predictive approaches for dementia that would reduce human bias, especially when it relates to diagnosis at the earliest stage of the disease wherein the clinical picture is vague. From this perspective, artificial intelligence and its division machine learning might be a possible solution for more accurate prediction and diagnosis of dementia in the future.

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KEY POINTS

- Machine learning is increasingly becoming more important in clinical decision-making in diagnosing and predicting of dementia with novel models achieving 90% of accuracy.
- There are still significant limitations of machine learning models, and conclusions and accuracy of detection and prediction provided by machine learning systems are only as good as the data that used to train the model.
- Currently, there are very few commercial applications of machine learning available.

Artificial intelligence is a field, which combines computer and data science, to enable problem-solving and to mimic the decision-making capabilities of the human mind [3]. Machine learning is a branch of artificial intelligence, a computational strategy that automatically determines (i.e. learns) methods and parameters from the data to reach an optimal solution to a problem rather than being programmed by a human to deliver a fixed solution [4,5]. Machine learning models may objectify the classification criteria, which potentially improve reliability and validity of assessments. Medical data often contain heterogeneous and multidimensional information with large amount of missing data that represent significant challenges for analyses using traditional statistical methods. In contrast, machine learning approaches are able to utilize this type of data for more accurate prediction of health outcomes [6▪▪]. Machine learning also offers reproducible and standardised instruments for studying multivariate datasets and identifying new patterns in large amount of clinical data. It facilitates automation of analyses, identifies and classifies patterns based on the conception that the computational model can learn to predict individualised outcomes. Machine learning is often a personalized rather than populational approach. Among the most well known machine learning applications are Support Vector Machines (SVM), Neural Networks, Decision Tree and Random Forest [4]. Deep learning is one of the emerging machine learning techniques that is increasingly often used in medicine to support in diagnosis of diseases and drug discovery [7]. Deep learning methods support automatic feature extraction and do not require to extract feature separately unlike other ML techniques. Convolutional Neural Networks (CNN) is the most widely used and explored, but there are also other machine learning architectures recently designed in the field, such as Deep Neural Network (DNN), Recurrent Neural Network (RNN), Deep Auto Encoder, Deep Belief Network (DBN) and Deep Boltzmann Machine (DBM) [7,8].

Application of machine learning technologies in medicine requires collaboration of different specialists including engineers, data scientists as well as medical professionals for formulating and testing hypotheses and insights [9]. First candidates for application of machine learning techniques in medicine are areas such as radiology, with large image datasets, wherein deep learning could characterize image patterns using [10]. However, psychiatry and psychogeriatrics may also benefit from application of machine learning technologies, such as artificial intelligence in different areas, including robotics technology and treatment support of individuals with mental disorders, such as autism, dementia and other conditions [11].

PREDICTION AND DETECTION OF DEMENTIA

The prediction and detection of dementia at the earliest stages is significant focus of current research worldwide [12,13]. Although there is no cure yet for the disease, prediction of mild cognitive impairment (MCI) and dementia is important to facilitate regarding decision-making (e.g. healthcare, financial or legal) while people still retain decision-making capacity. It also allows patients and families to receive care at an earlier stage in the disease process and may lead to improved disease prognosis and decreased morbidity. Therefore, machine learning technologies are increasingly becoming important tools in recognizing dementia risks and predicting its onset. There is a rise of research on prediction and identification of dementia that applies machine learning. An initial literature search using key words ‘machine learning dementia’ located about 6900 references published in 2017, and the number of publications almost doubled in 2020 approaching 12000.

DATASETS AVAILABLE FOR EXPLORING DEMENTIA

The majority of studies exploit publicly available datasets containing both neuroimaging and clinical data [14▪▪]. To be successful, machine learning algorithms need to be trained on a big amount of data. However, the number of datasets tailored to derive exclusively dementia-related information is currently limited. The most widely used datasets to explore dementia and Alzheimer’s disease are those based on MRI and electroencephalogram (EEG). For instance, there are the Alzheimer’s Disease Neuroimaging Initiative (ADNI) started in 2004 [15]; Open

Access Series of Imaging Studies (OASIS) [16]; the Minimal Interval Resonance Imaging in Alzheimer's Disease (MIRIAD) [17]; the Australian Imaging, Biomarkers and Lifestyle (AIBL) [18]; Chosun University Hospital (GUH) and Gwangju Optimal Dementia Center (GODC) datasets [19]. Another large study is the English Longitudinal Study of Aging (ELSA), which is a panel study of people living in England of longitudinal data from the 50+ English population that began in 2002. There are a few recent studies exploring individual and social factors in distinct age groups from the ELSA cohort that apply machine learning methods, but our search did not retrieve suitable studies/results of application of machine learning methods towards detection and prediction of dementia using the ELSA data. One of the most recent internationally recognized datasets is community-based cohort Sydney Memory and Ageing Study (MAS) commenced in 2005, which comprises clinical, neuroimaging and psychometric data [20]. There is also an electronic health record (EHR) data from the OptumLabs Data Warehouse (OLDW) that contains demographics information about people with dementia across the USA [21]. Among all of the datasets ADNI is the most widely used dataset to date [14▪▪].

APPLICATION OF ARTIFICIAL INTELLIGENCE TECHNOLOGIES IN DEMENTIA RESEARCH

Application of machine learning algorithms aims at detection (i.e. classification, support in diagnosis) and prediction of events [22▪]. Many studies developed and applied machine learning techniques for prediction and detection of dementia [14▪▪,23▪,24▪,25–27].

Both traditional and deep learning methods are used to distinguish between dementia and nondementia cases [28▪▪]. Zhu *et al.* [23▪] applied the machine learning Naive Bayes algorithm to an informant-based questionnaire of 5272 participants that showed good accuracy (81%) and precision (82%) with recall equal 81% and F-measure of 0.81. Another study reported the range of accuracy of different machine learning methods from 81 to 90%: SVM (87%), K-Nearest Neighbors (KNN) (84%), Linear Discriminant Analysis (LDA) (83%), Random Forest (88%), AdaBoost (81%) and XgBoost (90%) [22▪]. Applying deep learning models instead of machine learning methods is more costly in terms of run times and hardware requirements, but deep learning models outperform traditional machine learning models and can achieve accuracy over 90% in detection of dementia [14▪▪,29▪,30▪,31,32]. Nori *et al.* [29▪] used de-identified EHR data from the OLDW and developed a classification model to identify individuals with Alzheimer's disease and mild cognitive impairment. This incident model produced an AUC of 94.4% and F1 score of 54.1% [21]. Another group applied Multi-Layer Perceptron (MLP1 and MLP2) models and a Convolutional Bidirectional Long Short-Term Memory (ConvBLSTM) model for classification of MCI and dementia cases and reported accuracy of 86% [33]. Compared with other deep learning models, CNN achieved better accuracy and are currently most widely used for classification/detection purposes, preferably with an automatic multimodal longitudinal approach [7,34▪▪].

Most recent applications of machine learning are aimed at using psychometric and clinical data as well as MRI and PET datasets [28▪▪]. A systematic review and meta-analysis retrieved 17 studies that applied PET for the amyloid tracers using deep learning methods with pooled AUC of 96% [35▪]. There is also a relatively cheap EEG method available, which may be uniquely useful in the at-risk and presymptomatic phase of the dementia and for the detection of different cognitive conditions from normative aging to MCI and dementia [36▪▪,37▪,38]. This method demonstrated sound accuracy from 91% for MCI cases, 92% for dementia and 94.7% for cognitively normal individuals [37▪]. The majority of the recent studies focus on Alzheimer's disease detection incorporating SVM while underestimating deep learning usefulness for EEG data [39▪]. One study compared different machine learning and deep learning models and reported that the MLP classifier outperformed all other models, specifically, the Autoencoder, Logistic Regression and SVM [30▪]. They also found that CNN demonstrated 85.8% accuracy in discriminating between Alzheimer's disease vs. cognitively healthy individuals and lower accuracy for distinguishing between Alzheimer's disease vs. MCI (69.0%) and MCI vs. cognitively healthy individuals (85.3%) [40].

Deep learning methods are often able to achieve better accuracy for prediction of diseases including dementia [41,42▪,43]. For example, a recent study applied Variational Quantum Classification (VQC) in IBM's framework Qiskit, which outperformed SVM in accuracy of predicting dementia [41]. Australian researchers developed models that predict survival to dementia using baseline data from ADNI and MAS cohorts and applying the concordance index to measure performance. Their models achieved maximum performance values: 82% for MAS and 93% for ADNI [44▪▪]. Another recent study focused on prediction and detection of dementia using a new type of artificial intelligence named NeuCube, which applies neuromorphic, brain-like information processing principles and enables classification and deep learning of complex temporal and spatiotemporal data [6▪▪]. This methodology was applied to longitudinal MRI dataset derived from the MAS study spanning 6 years of follow-up [20], and accurately classified and predicted MCI and dementia 2 years ahead with 95 and 91% accuracy, respectively [6▪▪].

Alternative application of ML on nonneuroimaging data was performed by Shimoda *et al.* employing a machine learning predictive model based on extreme gradient boosting (XGBoost), Random Forest and logistic regression to identify Alzheimer's disease risk using rich voice audio data files of daily conversations. Predictive performance of the machine learning computational model was comparable to a classification method based on the Japanese version of the Telephone Interview for Cognitive Status (TICS-J) [45▪]. Another interesting study applied a combined methodology of machine learning and semi-parametric survival analysis to estimate the relative importance of 52 demographic, clinical and psychometric variables in predicting cognitive impairment and dementia in a population-representative sample ($n = 9979$) of older adults aged 50–98 years. Curiously, the researchers found that social-demographic and health variables (subjective health, BMI and emotional distress) were stronger predictors of cognitive impairment and dementia compared with clinical and behavioural indicators, such as cardiovascular factors (e.g. smoking, physical inactivity) and polygenic scores (e.g. APOE ε4) [46].

A promising area of application of machine learning is to analyse the functional health of individuals in their home environment and to assist people with dementia in their daily life activities. It can be done through the Internet of Things (IoT) solution as a smart home provides an opportunity to assess the functional health ability of individuals and it can be applied to older people with cognitive impairment in performing daily life activities. Javed *et al.* [47▪▪] proposed an approach named Cognitive Assessment of Smart Home Resident (CA-SHR) to detect cognitively impaired individuals in their early stages by measuring the ability of the resident to execute different daily living activities using predefined scores defined by a neuropsychologist and measuring the quality of tasks performed using supervised classification. A machine learning AdaBoost approach proposed by the authors resulted in 95% of classification accuracy [47▪▪].

ARTIFICIAL INTELLIGENCE ON THE MARKET

Commercial artificial intelligence products for dementia available in clinical facilities and applied sciences are limited as significant limitations of application of machine learning may not have been addressed yet. Artificial intelligence also imposes significant challenges in obtaining regulatory approval, which is a prerequisite of start usage of the technology in such strictly regulated areas as healthcare. Also, there is no systematic breakdown and classification of increasingly large and growing variety of artificial intelligence models. In recent years, however, there has been a considerable development of artificial intelligence based methods, which was prompted by the Food and Drug Administration's (FDA's) 'action plan' for artificial intelligence/machine learning based software as a medical device (SaMD) [48▪]. One of the areas where artificial intelligence technologies can be applied is dementia MRI diagnostics using quantitative volumetric reporting tools (QReports). QReports may help neuroradiologists to recognise and interpret the severity of brain atrophy by automatically computing an individual's brain volumes and comparing them against healthy populations [48▪,49–51]. Pemberton *et al.* [48▪] in their systematic review identified 17 such products, however, only four of them published clinical validation of their QReports in a dementia population.

In addition, there are several mobile apps available, which are mostly focused on screening for dementia and supporting individuals already diagnosed with MCI and dementia [52▪▪]. Very few of the apps (ACE-Mobile, MOBI-COG and Cognity) use machine learning solutions: ACE-Mobile and MOBI-COG exploit classifiers such as K-NN, mostly to reduce the error of the screening process, while Cognity is the only app that uses artificial intelligence technology to screen for Alzheimer's disease by analysing a photo of a clock drawing test done by the user in combination with the Mental Status Examination (MSE) tool that results in sensitivity and specificity ranges 71–92 and 52–96%, respectively [52▪▪]. One of the recently developed and scientifically robust risk assessment and motivational tools for stroke and accompanied noncommunicable diseases (NCDs) is the Stroke Riskometer mobile app [53▪]. It estimates personal stroke risk level and additional risk factors, including family medical history, cognitive impairment, memory loss and dementia. The Stroke Riskometer app was cross-culturally validated using Generalizability Theory and its risk assessment scores were found generalizable across countries and languages [54▪].

LIMITATIONS OF MACHINE LEARNING APPROACHES IN DEMENTIA

Despite many studies on application of ML to diagnosis and prediction of dementia, machine learning models are currently underdeveloped and have significant limitations. Researchers usually exploit the same datasets and most of the studies were conducted on a limited number of clinical sites and populations (e.g. cohort sizes 0–1000 patients) [14■■,23■]. Lack of systematic classification of the different artificial intelligence models with about 12 000 articles published on this topic in 2020 alone may affected inclusiveness of this review. Also, medical data usually imbalanced, subject of bias and contain significant amount of features accompanied by limited number of cases, which imposes additional challenges for analyses using machine learning methods often resulting in the inability to test causality and reverse causation. Therefore, the results may not represent real-world data because the performance of machine learning algorithms depend on the size of the training cohort [14■■]. Also, imbalanced sample sizes in the training datasets for each class label (diagnosis) impose additional limitations on robustness and clinical applicability of results [23■].

An important limitation of machine learning / deep learning models applied in health sciences is lack of meaningful interpretation of the results produced by machine learning models from the fundamental statistical perspective. For instance, an importance of each variable can be evaluated by their unique contribution to the health outcome in multiple linear regression model, which provides a beta coefficient and *p-value* for each variable that is statistically interpretable. However, machine learning models (e.g. Random Forest) may only rank the variables in order of their relative importance, without providing a P value or other cut-off point to separate the relevant and the irrelevant variables. Such information is important for clinicians, but machine learning models are currently unable to adequately address this issue. Reproducibility of research is also impaired by inconsistency of data formats between different institutions. Future studies should consider using common data models of standardized publicly available EHRs systems and specification of implementation details [14■■]. Another significant limitation is the course of the disease (especially on the initial stages) may vary, which along with the conceptual overlap of the Diagnostic and Statistical Manual of Mental Disorders (DSM) neurocognitive domains may lead to further potential diagnostic inaccuracy of the diseases [52■■]. Therefore, conclusions and accuracy of detection and prediction of the disease provided by machine learning systems are only as good as the data that used to train the model.

CONCLUSION

Although the best ML medical tool is still the doctor's brain, artificial intelligence is stepping in and increasingly becoming more important in clinical decision-making [55■]. The early and precise prediction and detection of dementia is still challenging for both medical professionals and researchers, and in the future deep learning methods in the hybridization of nature-inspired techniques should be explored for more effective diagnosis and prediction of dementia [7]. However, significant changes appear on the way with growing databanks containing the big data that are currently collected and processed.

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Conflicts of interest

There are no conflicts of interest.

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