Cureus

Diagnostic Efficacy and Clinical Relevance of Artificial Intelligence in Detecting Cognitive Decline

Ali A. Mohamed [1, 2] , Oge Marques [3, 2]

1. Neurological Surgery, Charles E. Schmidt College of Medicine, Florida Atlantic University, Boca Raton, USA   2. Electrical Engineering and Computer Science, Florida Atlantic University, Boca Raton, USA   3. Biomedical Sciences, Charles E. Schmidt College of Medicine, Florida Atlantic University, Boca Raton, USA

Corresponding author: Ali A. Mohamed, amohamed2020@health.fau.edu

Abstract

Cognitive impairment is an age-associated disorder of increasing prevalence as the aging population continues to grow. Classified based on the level of cognitive decline, memory, function, and capacity to conduct activities of daily living, cognitive impairment ranges from mild cognitive impairment to dementia. When considering the insidious nature of the etiologies responsible for varying degrees of cognitive impairment, early diagnosis may provide a clinical benefit through the facilitation of early treatment. Typical diagnosis relies heavily on evaluation in a primary care setting. However, there is evidence that other diagnostic tools may aid in an earlier diagnosis of the different underlying pathologies responsible for cognitive impairment. Artificial intelligence represents a new intersecting field with healthcare that may aid in the early detection of neurodegenerative disorders. When assessing the role of AI in detecting cognitive decline, it is important to consider both the diagnostic efficacy of AI algorithms and the clinical relevance and impact of early interventions as a result of early detection. Thus, this review highlights promising investigations and developments in the space of artificial intelligence and healthcare and their potential to impact patient outcomes.

Introduction And Background

With a current report of over 700 million people 65 years of age or older in 2020 and an anticipated doubling of the number of people within this age group in the United States by 2050, it is important to consider the current and anticipated prevalence of certain diseases and disabilities [1]. Cognitive impairment is one specific age-associated disorder to consider.

Cognitive impairment, defined as a decline in cognitive function, can be classified based on the severity of cognitive decline, loss of learning and memory capacity, and dependence on conducting activities of daily living [2,3]. Beyond normal age-related manifestations, cognitive dysfunction ranges from mild cognitive impairment (MCI) to dementia. MCI is identified as a decline in memory and other cognitive abilities [4]. Dementia is identified as a more severe neurocognitive impairment, with a decline in memory, problem-solving, language, and other higher-level cognitive abilities [5]. MCI is clinically described as a transitional phase between normal age-related manifestations and dementia [4]. Progression to dementia from MCI has been estimated to occur in 10% of cases annually [6]. The onset of primary dementia follows a slow progression as the underlying pathology takes its course. The main underlying etiologies, and therefore causes of dementia, include Alzheimer's disease, frontotemporal dementia, Lewy body disease, and Parkinson's disease. Vascular dementia, traumatic brain injury, Huntington's disease, stroke, and prion disease represent other neurodegenerative etiologies of progressive cognitive dysfunction and dementia [7-11].

Because of the insidious nature of neurodegenerative disease, many investigations have focused on early diagnosis and intervention in hopes of improving outcomes for patients [12,13]. Studies have identified the role of lifestyle modification, risk factor mitigation, and early pharmacological intervention in the suppression of disease progression [14,15]. The literature continues to suggest that improved diagnostic capacity, allowing for early intervention, is critical in providing patients with the best outcomes [16,17].

Diagnostic tools for cognitive impairment for many etiologies of dementia include neurocognitive testing, imaging, cerebrospinal fluid assessment, and biomarker tracking [13,18]. However, despite the availability of technical diagnostic methods, typical evaluation of dementia is appropriately done in the primary care setting. Diagnosis is based primarily on the patient's medical history, with input from close family and friends, followed by a cognitive and neurological examination as indicated. Considering the subtle nature of neurocognitive decline, it is reasonable to conclude that screening tools should be established to ensure early detection and treatment. The 2020 US Preventative Services Task Force came to a similar conclusion, noting that there was evidence for establishing high specificity and sensitivity screening tools for the identification of dementia. However, the overall conclusion was that there remains insufficient evidence to

balance the harms and benefits of cognitive impairment screening [19].

Despite uncertainty on asymptomatic screening, with a predilection away from doing so, screening patients experiencing memory difficulties and other suggestive symptoms is generally accepted. Beyond screening based on a patient's medical history, new novel tools have been explored for evaluation, early detection, and intervention. These include eye tracking devices, peripheral blood-based measures/biomarkers, passive assessments of cognition using smartphone and tablet devices, remote cognitive assessments, and repeatable remote brain assessment using electroencephalography (EEG) [20,21]. Artificial intelligence (AI) is a rapidly growing field that intersects with medicine on many fronts. Previous investigations have specifically explored the role of AI in the detection of neurocognitive and neurodegenerative diseases [22,23]. Other investigations suggest that AI can be leveraged to establish a plan of care for at-risk patients with different forms of neurodecline [24-28]. Ultimately, the role of AI in health care and specifically in diagnosing patients with neurodegenerative disorders remains unknown to many clinicians. Furthermore, it is unclear if earlier detection using AI algorithms sufficiently changes patient outcomes. Thus, we present this review to highlight the capacity of AI in the early detection of neurodegenerative disorders and to discuss the evidence regarding early intervention and its impact on patient outcomes. In this review, we aim to clarify if AI's capacity for early detection is worth the investment of resources based on how impactful early intervention is on patient outcomes. Many investigations have demonstrated suboptimal outcomes, however, the focus of this review will be to highlight promising investigations and developments in the space of artificial intelligence and healthcare and their potential to impact patient outcomes.

Review

Mild cognitive impairment (MCI)

MCI represents a predementia phase of disease in patients with symptomatic cognitive and functional impairment. Although primarily focused on Alzheimer's disease being the underlying pathological basis of the intermediate level of impairment, many other neurodegenerative disorders have been implicated for MCI in more recent investigations [29-31].

Several studies have explored the use of AI machine-learning models for the detection of MCI (Table 1). One study specifically leverages the abnormal patterns of emotion and difficulties with facial muscle control found in patients with MCI [32-35]. Fei et al. utilized a Support Vector Machine model for MCI detection in the early stages [36]. They demonstrated a detection accuracy of 73.3%.

Reference	Disorder	AI model	Training modality	Accuracy
Fei et al. (2022) [36]	MCI	SVM, MobileNet	Facial expressions	73.30%
Kang et al. (2019) [37]	MCI	ANN	NPT data	96.66%
Boettcher et al. (2020) [38]	MCI, AD	SVM	Clinical data	77.17%
Ghoraani et al. (2021) [39]	MCI, AD	SVM	Clinical data	91%
Goenka and Tiwari (2022) [40]	AD	CNN	MRI	98.30%
Almubark et al. (2020) [41]	AD	MLP	Cognitive data	92.98%
Fulton et al. (2019) [42]	AD	GBM, ResNet-50	MRI	99%
Odusami et al. (2022) [43]	AD	DenseNet201, ResNet18	MRI	98.86%
Pan et al. (2020) [44]	AD	CNN	MRI	84%
Hazarika et al (2022) [45]	AD	DNN, DenseNet, Residual Networks, Inception-V1, V2, V3	MRI	90.22%
Mathotaarachchi et al. (2017) [46]	AD	RUSRF	MRI, PET	84%
Naganandhini et al. (2019) [47]	AD	DTC-HPT	MRI	99%
Pekkala et al. (2017) [48]	AD	SVM	MRI, CT, Clinical data	95%
Bron et al. (2014) [49]	AD	Linear SVM	MRI, PET	89-90%
Herzog et al. (2021) [50]	AD	SVM, KNN, LD, NB	MRI	77-93%
Venugopalan et al. (2021) [51]	AD	SVM, KNN, DL, RF, DT	MRI, Clinical data	68-89%
Battineni et al. (2020) [52]	AD	SVM, RF, GBM, AdaBoosting, LR, NB	MRI	95.96-97.58%
El-Sappagh et al. (2021) [53]	AD	RF	MRI	94.40%

Shimoda et al. (2021) [54]	AD	RF, LR, XGBoost	Clinical data	86.3-89.3%
Sabry et al. (2022) [55]	AD	SVM, KNN, LR, LDA	Clinical data	90.1-91.8%
Miltiadous et al. (2021) [56]	AD	SVM, KNN, RF, DT, ANN, NB	EEG	80-99.1%
Danso et al. (2021) [57]	AD	RF, XGBoost	Clinical data	85-87%
Byeon (2020) [58]	AD, PD	RF	MRI	73.30%
Ni et al. (2021) [59]	LBD, AD	ResNet-50	SPECT	71-90%
Bougea et al. (2022) [60]	LBD, PD	SVM, KNN, binomial logistic regression, NB, Ensemble	Clinical data	82.05-91.2%
Boutet et al. (2021) [61]	PD	ML model	MRI	88%
Signaevsky et al. (2022) [62]	PD	CNN	WSI	99%
Juutinen et al. (2020) [63]	PD	SVM, RF, KNN, LR, LDA, NB, Classification tree, Ensemble, Gaussian Kernel	Clinical data	74.1-84.5%
Hu et al. (2021) [64]	FTD, AD	CNN	MRI	89.86-93.45%
Garcia-Gutierrez et al. (2022) [65]	FTD, AD	SVM, KNN, GBM, DT, NB, RF	PET, Clinical data	82.9-85.4%

TABLE 1: Overview of papers utilizing artificial intelligence for early detection of neurodegenerative disorders.

MCI: mild cognitive impairment; AD: Alzheimer's disease; PD: Parkinson's disease; LBD: Lewy body dementia; FTD: frontotemporal dementia; SVM: support vector machines; ANN: artificial neural network; CNN: convolutional neural network; MLP: multilayer perceptron; GBM: gradient boosting machine; RUSRF: random under-sampling random forest; DTC-HPT: decision trees classifier hyperparameter tuning; KNN: k-nearest neighbors classifier; LD: linear discriminant; NB: Naïve Bayes; DL: deep learning; RF: random forest; DT: decision trees; ML: machine learning; NPT: non-linear projection trick; MRI: magnetic resonance imaging; PET: positron emission tomography; CT: computerized tomography; EEG: electroencephalogram; SPECT: single-photon emission computed tomography; WSI: whole-slide images

Kang et al. utilized the Seoul Neuropsychological Screening Battery, a tool commonly used in Korea for cognitive function assessment in patients with neurological disorders, to develop an algorithm for differentiating and therefore detecting cognitive impairment in patients [37]. Their model demonstrated 79% accuracy in the three-way classification of normal cognition vs. MCI vs. Alzheimer's disease dementia and 96.66% accuracy in the detection of MCI.

Boettcher et al. and Ghoraani et al. both conducted investigations for the detection of MCI using gait data from the dual-task assessment. With the use of a Support Vector Machine and gradient tree boosting machine learning models, they demonstrated an accuracy of MCI detection ranging from 78% to 81.52% [38,39].

With promising developments in AI-based early detection of MCI, it is reasonable to anticipate better outcomes for patients because of the capacity for early intervention. Despite no specific treatment for MCI, there is evidence suggesting the benefits of early intervention. Memory training and cognitive training have both demonstrated improvements in memory functioning and enhanced brain activity on neuroimaging [66-68]. Previous research has also demonstrated the capacity of traditional Chinese medicines to delay the transition to Alzheimer's disease from MCI [69]. Considering the evidence of improved outcomes with earlier intervention, advancements in AI for the detection of MCI have the potential to play a major role in the overall care of patients experiencing neurocognitive decline.

Alzheimer's disease (AD)

AD is a neurodegenerative disorder responsible for the majority of cases of adult-onset dementia [70]. Initially presenting with mild symptoms of short-term memory loss, as AD progresses, patients experience a gradual loss of memory, changes in personality, and other changes in brain function including problem-solving, executive functioning, and judgment [71]. The literature regarding the use of AI for the diagnosis of neurodegenerative decline majorly focuses on AD (Table 1). Almost all previous works utilized AI in conjunction with imaging and/or cognitive datasets.

Goenka and Tiwari utilized a deep convolutional neural network technique with the incorporation of regularization algorithms to achieve three-class categorization of AD, MCI, and normal control whole brain volumetric scans [40]. They demonstrated an accuracy of 98.26% in differentiating between the three classes of neurocognition. Another study utilized convolutional neural networks and deep learning for early

diagnosis of AD with accuracy ranging from 93.61% to 97% respective to stage classifications of the disorder within the paper [72]. Similarly, Almubark et al. demonstrated a 92.98% accuracy in diagnosing AD using cognitive data with convolutional neural networks [41]. Fulton et al. and Odusami et al. demonstrated nearly 100% accuracy in detection in their investigations for classifying AD stages with DenseNet and ResNet using the clinical dementia ratio and mini-mental state examination tests [42,43]. Many other studies have proposed novel approaches for early diagnosis of AD using magnetic resonance imaging (MRI) [44-53,58], and electroencephalogram (EEG) [38,39,54-57].

Evident by the number of investigations and the demonstration of high accuracy by the many different proposed algorithms, the use of AI as an aid for the early diagnosis of AD by future clinicians is a reasonable expectation as this area of research continues to grow and prove its efficacy. Despite no definitive treatment of AD, there is evidence that early treatment preserves cognition, behavior, and functional independence in patients. Early treatment with donepezil demonstrated cognitive stabilization and improvement in several control trials [73-76]. Others have demonstrated the efficacy of early treatment with cholinesterase inhibitors [77]. Many other treatment options are currently available for mild and severe cases of AD, but more investigations are required to assess their efficacy early on [78]. In either case, with the continuous introduction of new novel therapeutics for managing AD, early diagnosis is becoming increasingly important for optimizing patient outcomes. With this understanding, it is clear that advances in AI in healthcare, with respect to early diagnosis of AD, have the potential to play a major role in the overall management of patients experiencing this major category of neurocognitive and functional decline.

Frontotemporal dementia (FTD)

FTD is commonly underdiagnosed as symptoms of the disease overlap with different psychiatric manifestations. FTD clinically presents with features of behavior deficit, language deficits, and/or executive function decline [79]. Because of the overlap in clinical presentation, FTD is challenging to diagnose as it must be differentiated from AD and other etiologies of neurocognitive decline. Different algorithms have been explored on this front, but each has presented with different levels of difficulty (Table 1). Some investigations have specifically explored deep learning techniques for differentiating between FTD and AD, but the results remain inconclusive [64]. Deep-learning-assisted diagnostic investigations have demonstrated promising findings but are difficult to apply because they rely on expert-level pre-processing [80]. Genetic algorithms have been successful in differentiating between the two, mimicking etiologies of dementia using machine learning [65]. However, it is clear that further research is required before definitively understanding the potential role of AI in the early diagnosis of FTD.

Despite the necessity of growth in the intersection between AI and healthcare for the management of FTD, it is still crucial to understand if an early diagnosis, beyond what clinicians are currently capable of, could provide value to patients. Unfortunately, there is no indication that an early diagnosis would provide a benefit to patients. There are currently no treatment or management options to decrease the progression of FTD. Current management approaches focus on symptomatic treatment using off-label medications [81]. Although efficacious in some circumstances, there is limited control trial evidence supporting the use of these medications. Furthermore, these medications are not expected to play a role in minimizing the progression of the disease because they do not target the underlying pathophysiology of FTD [82-89]. With an unclear understanding of management and treatment options for patients with FTD, it is not expected that the use of AI for early detection will play a relevant role in patient care. However, if novel treatment approaches demonstrate efficacy at early points of disease presentation, the use of AI for early diagnosis should be explored.

Parkinson's disease (PD)

PD is a neurodegenerative disorder characterized by bradykinesia and the presence of a resting tremor, rigidity, or similar symptom. PD is a progressive disorder but has a slow onset. Patients typically present with tremors, followed by cardinal features of rigidity and bradykinesia [90,91]. Boutet et al. utilized MRI for the implementation of a machine-learning model for the detection of PD [61]. Signaevsky et al. utilized whole slide images for the implementation of a conventional neural network for the detection of PD [62]. Others have developed algorithms for PD detection with the incorporation of clinical data [55,63] and MRI [58]. Accuracy ranges for these investigations were from 74% to 99% (Table 1). Despite a wide range in accuracy across these investigations, reasonable strides have been made to demonstrate the utility of AI in the early detection of PD. To evaluate the relevance AI will have in patient management, the impact of early detection on outcomes of patients with PD needs to be explored.

Previous literature has established that early treatment of PD is crucial in slowing both the progression and symptomatic manifestations of the disease. Targeted for the management of motor and non-motor symptoms, clinical trials have studied the efficacy of early intervention of PD using rasagiline, ropinirole, pramipexole, and rotigotine [92-95]. However, an important and specific consideration must be made regarding the initiation of early intervention in patients with PD. Many therapeutic options for these patients come with a reasonable risk of additional side effects [96,97]. Outside of pharmacological treatment, physical therapy, speech therapy, and exercise are all early interventions for effective symptom management [98].

Considering the efficacy of early pharmacological and non-pharmacological treatment options for patients with PD, early detection plays a relevant role. Because of this, the role of AI in the early detection of PD is

clinically relevant and will likely grow in importance as future investigations demonstrate more streamlined and efficient approaches compared to the current diagnostic standard.

Lewy body dementia (LBD)

LBD is a progressive neurodegenerative disorder that clinically presents with features of both dementia and PD. Typically, patients will present with dementia prior to motor signs and visual hallucinations [99]. Similarly to what has been discussed in the case of FTD, LBD is challenging to diagnose because of its clinical similarities to many different etiologies of dementia. Differentiation of LBD from AD has been achieved using deep learning models leveraging medical experience as a concatenation layer [60]. Other investigations have capitalized on machine learning algorithms that rely on easily attainable, non-invasive predictors such as imaging and patient surveys [59,100]. Accuracy for the discussed investigations ranged from 82.05% to 91.2% (Table 1). Although the literature is modest in this subtype of neurodegenerative decline, findings suggest a reasonable role for AI in the early detection of LBD. However, the clinical relevance of early detection depends on the efficacy of early treatment.

Early intervention for patients with LBD is imperative because it is most responsive early in its disease course [101]. The efficacy of early treatment of LBD has been demonstrated with memantine, rivastigmine, olanzapine, and Yokukansan [102,103]. Of the discussed etiologies of neurocognitive decline, early detection with AI may be most beneficial in the context of LBD. Because of the importance of early intervention and treatment, earlier detection of LBD is critical in optimizing outcomes for patients and improving the quality of care.

Conclusions

The impact of early treatment for different pathologies responsible for cognitive decline emphasizes the importance of early detection for maximizing patient outcomes. The role of AI in the early detection of cognitive decline is becoming increasingly relevant as novel algorithms continue to demonstrate increased levels of efficacy. However, it is important to recognize that many factors, such as differences in data set size and modalities, reduce the reproducibility of the findings of these studies. It is also important to recognize that reported accuracy may not be the best figure to demonstrate the efficacy of the proposed AI models in detecting neurodegenerative disease. In addition, the lack of clinical application makes it unclear how truly feasible and efficacious these models are. Lastly, the role of early detection, and therefore the role of AI algorithms in that space, may not currently be relevant, regardless of model efficacy, in pathologies with no definitive treatment or evidence of improved outcomes with early intervention. Despite this, future investigations should continue to explore the efficacy of early treatment for all pathologies and the role of AI in the early detection of these pathologies to facilitate earlier intervention.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Ali A. Mohamed, Oge Marques

Drafting of the manuscript: Ali A. Mohamed

Critical review of the manuscript for important intellectual content: Ali A. Mohamed, Oge Marques

Supervision: Oge Marques

Disclosures

References

1. World population ageing 2020. (2020). https://www.un.org/development/desa/pd/sites/www.un.org.development.desa.pd/files/files/documents/2020/Sep/un_pop_2...
2. Wang S, Zhang J, Liang J, Song H, Ji X: Treatable causes of adult-onset rapid cognitive impairment . Clin Neurol Neurosurg. 2019, 187:10.1016/j.clineuro.2019.105575
3. Chertkow H: Diagnosis and treatment of dementia: introduction. Introducing a series based on the Third Canadian Consensus Conference on the diagnosis and treatment of dementia. CMAJ. 2008, 178:316-21. 10.1503/cmaj.070795
4. Duff K: Mild cognitive impairment and dementia: definitions, diagnosis, and treatment . Arch Clin Neuropsychol. 2014, 29:691-2. 10.1093/arclin/acu034

5. Spiegel D, Loewenstein RJ, Lewis-Fernández R, et al.: Dissociative disorders in DSM-5 . Depress Anxiety. 2011, 28:824-52. 10.1002/da.20874

6. Busse A, Angermeyer MC, Riedel-Heller SG: Progression of mild cognitive impairment to dementia: a challenge to current thinking. Br J Psychiatry. 2006, 189:399-404. 10.1192/bjp.bp.105.014779

7. Ferencz B, Gerritsen L: Genetics and underlying pathology of dementia . Neuropsychol Rev. 2015, 25:113-24. 10.1007/s11065-014-9276-3

8. Aarsland D: Epidemiology and pathophysiology of dementia-related psychosis . J Clin Psychiatry. 2020, 81:10.4088/JCP.AD19038BR1C

9. Dening T, Sandilyan MB: Dementia: definitions and types. Nurs Stand. 2015, 29:37-42. 10.7748/ns.29.37.37.e9405

10. Vahia VN: Diagnostic and statistical manual of mental disorders 5: a quick glance . Indian J Psychiatry. 2013, 55:220-3. 10.4103/0019-5545.117131

11. Roh JH, Lee JH: Recent updates on subcortical ischemic vascular dementia . J Stroke. 2014, 16:18-26. 10.5853/jos.2014.16.1.18

12. Arevalo-Rodriguez I, Smailagic N, Roqué-Figuls M, et al.: Mini-mental state examination (MMSE) for the early detection of dementia in people with mild cognitive impairment (MCI). Cochrane Database Syst Rev. 2021, 7:10.1002/14651858.CD010783.pub3

13. Jack CR Jr, Bennett DA, Blennow K, et al.: NIA-AA research framework: toward a biological definition of Alzheimer's disease. Alzheimers Dement. 2018, 14:535-62. 10.1016/j.jalz.2018.02.018

14. Maki Y, Yamaguchi H: Early detection of dementia in the community under a community-based integrated care system. Geriatr Gerontol Int. 2014, 14:2-10. 10.1111/ggi.12259

15. Orgeta V, Mukadam N, Sommerlad A, Livingston G: The Lancet Commission on dementia prevention, intervention, and care: a call for action. Ir J Psychol Med. 2019, 36:85-8. 10.1017/ipm.2018.4

16. Carotenuto A, Traini E, Fasanaro AM, Battineni G, Amenta F: Tele-neuropsychological assessment of Alzheimer's disease. J Pers Med. 2021, 11:10.3390/jpm11080688

17. Battineni G, Hossain MA, Chintalapudi N, Traini E, Dhulipalla VR, Ramasamy M, Amenta F: Improved Alzheimer's disease detection by MRI using multimodal machine learning algorithms. Diagnostics (Basel). 2021, 11:10.3390/diagnostics11112103

18. McKhann GM, Knopman DS, Chertkow H, et al.: The diagnosis of dementia due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers Dement. 2011, 7:263-9. 10.1016/j.jalz.2011.03.005

19. Owens DK, Davidson KW, Krist AH, et al.: Screening for cognitive impairment in older adults: US Preventive Services Task Force recommendation statement. J Am Med Assoc. 2020, 323:757-63. 10.1001/jama.2020.0435

20. Tadokoro K, Yamashita T, Fukui Y, et al.: Early detection of cognitive decline in mild cognitive impairment and Alzheimer's disease with a novel eye tracking test. J Neurol Sci. 2021, 427:10.1016/j.jns.2021.117529

21. Whelan R, Barbey FM, Cominetti MR, Gillan CM, Rosická AM: Developments in scalable strategies for detecting early markers of cognitive decline. Transl Psychiatry. 2022, 12:10.1038/s41398-022-02237-w

22. Gaubert S, Houot M, Raimondo F, et al.: A machine learning approach to screen for preclinical Alzheimer's disease. Neurobiol Aging. 2021, 105:205-16. 10.1016/j.neurobiolaging.2021.04.024

23. Herraiz ÁH, Martínez-Rodrigo A, Bertomeu-González V, Quesada A, Rieta JJ, Alcaraz R: A deep learning approach for featureless robust quality assessment of intermittent atrial fibrillation recordings from portable and wearable devices. Entropy (Basel). 2020, 22:10.3390/e22070733

24. Landolfi A, Ricciardi C, Donisi L, et al.: Machine learning approaches in Parkinson's disease . Curr Med Chem. 2021, 28:6548-68. 10.2174/0929867328999210111211420

25. Merkin A, Krishnamurthi R, Medvedev ON: Machine learning, artificial intelligence and the prediction of dementia. Curr Opin Psychiatry. 2022, 35:123-9. 10.1097/YCO.0000000000000768

26. Agarwal D, Marques G, de la Torre-Díez I, Franco Martin MA, García Zapiraín B, Martín Rodríguez F: Transfer learning for Alzheimer's disease through neuroimaging biomarkers: a systematic review . Sensors (Basel). 2021, 21:10.3390/s21217259

27. Kumar S, Oh I, Schindler S, Lai AM, Payne PR, Gupta A: Machine learning for modeling the progression of Alzheimer disease dementia using clinical data: a systematic literature review. JAMIA Open. 2021, 4:10.1093/jamiaopen/ooab052

28. Tsang G, Xie X, Zhou SM: Harnessing the power of machine learning in dementia informatics research: issues, opportunities, and challenges. IEEE Rev Biomed Eng. 2020, 13:113-29. 10.1109/RBME.2019.2904488

29. Gorelick PB, Scuteri A, Black SE, et al.: Vascular contributions to cognitive impairment and dementia: a statement for healthcare professionals from the american heart association/american stroke association. Stroke. 2011, 42:2672-713. 10.1161/STR.0b013e3182299496

30. McKeith IG, Ferman TJ, Thomas AJ, et al.: Research criteria for the diagnosis of prodromal dementia with Lewy bodies. Neurology. 2020, 94:743-55. 10.1212/WNL.0000000000009323

31. Litvan I, Goldman JG, Tröster AI, et al.: Diagnostic criteria for mild cognitive impairment in Parkinson's disease: Movement Disorder Society Task Force guidelines. Mov Disord. 2012, 27:349-56. 10.1002/mds.24893

32. Henry JD, Rendell PG, Scicluna A, Jackson M, Phillips LH: Emotion experience, expression, and regulation in Alzheimer's disease. Psychol Aging. 2009, 24:252-7. 10.1037/a0014001

33. Burton KW, Kaszniak AW: Emotional experience and facial expression in Alzheimer's disease . Neuropsychol Dev Cogn B Aging Neuropsychol Cogn. 2006, 13:636-51. 10.1080/13825580600735085

34. Smith MC: Facial expression in mild dementia of the Alzheimer type . Behav Neurol. 1995, 8:149-56.

35. Chen KH, Lwi SJ, Hua AY, Haase CM, Miller BL, Levenson RW: Increased subjective experience of non-target emotions in patients with frontotemporal dementia and Alzheimer's disease. Curr Opin Behav Sci. 2017, 15:77-84. 10.1016/j.cobeha.2017.05.017

36. Fei Z, Yang E, Yu L, Li X, Zhou H, Zhou W: A novel deep neural network-based emotion analysis system for automatic detection of mild cognitive impairment in the elderly. Neurocomputing. 2022, 468:468-10. 10.1016/j.neucom.2021.10.038

37. Kang MJ, Kim SY, Na DL, et al.: Prediction of cognitive impairment via deep learning trained with multi-center neuropsychological test data. BMC Med Inform Decis Mak. 2019, 19:10.1186/s12911-019-0974-x

38. Boettcher LN, Hssayeni M, Rosenfeld A, Tolea MI, Galvin JE, Ghoraani B: Dual-task gait assessment and

2023 Mohamed et al. Cureus 15(10): e47004. DOI 10.7759/cureus.47004

6 of 9

machine learning for early-detection of cognitive decline. Annu Int Conf IEEE Eng Med Biol Soc. 2020, 2020:3204-7. 10.1109/EMBC44109.2020.9175955

39. Ghoraani B, Boettcher LN, Hssayeni MD, Rosenfeld A, Tolea MI, Galvin JE: Detection of mild cognitive impairment and Alzheimer's disease using dual-task gait assessments and machine learning. Biomed Signal Process Control. 2021, 64:10.1016/j.bspc.2020.102249

40. Goenka N, Tiwari S: AlzVNet: a volumetric convolutional neural network for multiclass classification of Alzheimer's disease through multiple neuroimaging computational approaches. Biomed Signal Process Control. 2022, 74:10.1016/j.bspc.2022.103500

41. Almubark I, Chang LC, Shattuck KF, Nguyen T, Turner RS, Jiang X: A 5-min cognitive task with deep learning accurately detects early Alzheimer's disease. Front Aging Neurosci. 2020, 12:10.3389/fnagi.2020.603179

42. Fulton LV, Dolezel D, Harrop J, Yan Y, Fulton CP: Classification of Alzheimer's disease with and without Imagery using gradient boosted machines and ResNet-50. Brain Sci. 2019, 9:10.3390/brainsci9090212

43. Odusami M, Maskeliūnas R, Damaševičius R: An intelligent system for early recognition of Alzheimer's disease using neuroimaging. Sensors (Basel). 2022, 22:10.3390/s22030740

44. Pan D, Zeng A, Jia L, Huang Y, Frizzell T, Song X: Early detection of Alzheimer's disease using magnetic resonance imaging: a novel approach combining convolutional neural networks and ensemble learning. Front Neurosci. 2020, 14:10.3389/fnins.2020.00259

45. Hazarika RA, Kandar D, Maji AK: An experimental analysis of different deep learning based models for Alzheimer's disease classification using brain magnetic resonance images. J King Saud Univ Comput Inf Sci. 2022, 34:8576-98. 10.1016/j.jksuci.2021.09.003

46. Mathotaarachchi S, Pascoal TA, Shin M, et al.: Identifying incipient dementia individuals using machine learning and amyloid imaging. Neurobiol Aging. 2017, 59:80-90. 10.1016/j.neurobiolaging.2017.06.027

47. Naganandhini S, Shanmugavadivu P: Effective diagnosis of Alzheimer's disease using modified decision tree classifier. Procedia Comput Sci. 2019, 165:548-55. 10.1016/j.procs.2020.01.049

48. Pekkala T, Hall A, Lötjönen J, et al.: Development of a late-life dementia prediction index with supervised machine learning in the population-based CAIDE study. J Alzheimers Dis. 2017, 55:1055-67. 10.3233/JAD-160560

49. Bron EE, Steketee RM, Houston GC, et al.: Diagnostic classification of arterial spin labeling and structural MRI in presenile early stage dementia. Hum Brain Mapp. 2014, 35:4916-31. 10.1002/hbm.22522

50. Herzog NJ, Magoulas GD: Brain asymmetry detection and machine learning classification for diagnosis of early dementia. Sensors (Basel). 2021, 21:10.3390/s21030778

51. Venugopalan J, Tong L, Hassanzadeh HR, Wang MD: Multimodal deep learning models for early detection of Alzheimer's disease stage. Sci Rep. 2021, 11:10.1038/s41598-020-74399-w

52. Battineni G, Chintalapudi N, Amenta F, Traini E: A comprehensive machine-learning model applied to magnetic resonance imaging (MRI) to predict Alzheimer's disease (ad) in older subjects. J Clin Med. 2020, 9:10.3390/jcm9072146

53. El-Sappagh S, Alonso JM, Islam SM, Sultan AM, Kwak KS: A multilayer multimodal detection and prediction model based on explainable artificial intelligence for Alzheimer's disease. Sci Rep. 2021, 11:10.1038/s41598-021-82098-3

54. Shimoda A, Li Y, Hayashi H, Kondo N: Dementia risks identified by vocal features via telephone conversations: a novel machine learning prediction model. PLoS One. 2021, 16:10.1371/journal.pone.0253988

55. Sabry F, Eltaras T, Labda W, Alzoubi K, Malluhi Q: Machine learning for healthcare wearable devices: the big picture. J Healthc Eng. 2022, 2022: 10.1155/2022/4653923

56. Miltiadous A, Tzimourta KD, Giannakeas N, Tsipouras MG, Afrantou T, Ioannidis P, Tzallas AT: Alzheimer's disease and frontotemporal dementia: a robust classification method of EEG signals and a comparison of validation methods. Diagnostics (Basel). 2021, 11:10.3390/diagnostics11081437

57. Danso SO, Zeng Z, Muniz-Terrera G, Ritchie CW: Developing an explainable machine learning-based personalised dementia risk prediction model: a transfer learning approach with ensemble learning algorithms. Front Big Data. 2021, 4:10.3389/fdata.2021.613047

58. Byeon H: Application of machine learning technique to distinguish Parkinson's disease dementia and Alzheimer's dementia: predictive power of Parkinson's disease-related non-motor symptoms and neuropsychological profile. J Pers Med. 2020, 10: 10.3390/jpm10020031

59. Ni YC, Tseng FP, Pai MC, et al.: The feasibility of differentiating Lewy body dementia and Alzheimer's disease by deep learning using ECD SPECT images. Diagnostics (Basel). 2021, 11:10.3390/diagnostics11112091

60. Bougea A, Efthymiopoulou E, Spanou I, Zikos P: A novel machine learning algorithm predicts dementia with Lewy bodies versus Parkinson's disease dementia based on clinical and neuropsychological scores. J Geriatr Psychiatry Neurol. 2022, 35:317-20. 10.1177/0891988721993556

61. Boutet A, Madhavan R, Elias GJ, et al.: Predicting optimal deep brain stimulation parameters for Parkinson's disease using functional MRI and machine learning. Nat Commun. 2021, 12:10.1038/s41467-021-23311-9

62. Signaevsky M, Marami B, Prastawa M, et al.: Antemortem detection of Parkinson's disease pathology in peripheral biopsies using artificial intelligence. Acta Neuropathol Commun. 2022, 10:10.1186/s40478-022-01318-7

63. Juutinen M, Wang C, Zhu J, Haladjian J, Ruokolainen J, Puustinen J, Vehkaoja A: Parkinson's disease detection from 20-step walking tests using inertial sensors of a smartphone: machine learning approach based on an observational case-control study. PLoS One. 2020, 15:10.1371/journal.pone.0236258

64. Hu J, Qing Z, Liu R, et al.: Deep learning-based classification and voxel-based visualization of frontotemporal dementia and Alzheimer's disease. Front Neurosci. 2020, 14:10.3389/fnins.2020.626154

65. García-Gutierrez F, Díaz-Álvarez J, Matias-Guiu JA, Pytel V, Matías-Guiu J, Cabrera-Martín MN, Ayala JL: GA-MADRID: design and validation of a machine learning tool for the diagnosis of Alzheimer's disease and frontotemporal dementia using genetic algorithms. Med Biol Eng Comput. 2022, 60:2737-56. 10.1007/s11517-022-02630-z

66. Belleville S, Clément F, Mellah S, Gilbert B, Fontaine F, Gauthier S: Training-related brain plasticity in subjects at risk of developing Alzheimer's disease. Brain. 2011, 134:1623-34. 10.1093/brain/awr037

67. Li H, Li J, Li N, Li B, Wang P, Zhou T: Cognitive intervention for persons with mild cognitive impairment: a

2023 Mohamed et al. Cureus 15(10): e47004. DOI 10.7759/cureus.47004

7 of 9

meta-analysis. Ageing Res Rev. 2011, 10:285-96. 10.1016/j.arr.2010.11.003

68. Gates NJ, Sachdev PS, Fiatarone Singh MA, Valenzuela M: Cognitive and memory training in adults at risk of dementia: a systematic review. BMC Geriatr. 2011, 11: 10.1186/1471-2318-11-55

69. Zhong J, Tian J, Zhu A, Yang C: Clinical study on a randomized, double-blind control of Shenwu gelatin capsule in treatment of mild cognitive impairment. [Article in Chinese]. Zhongguo Zhong Yao Za Zhi. 2007, 32:1800-3.

70. Alzheimer's Association: 2016 Alzheimer's disease facts and figures . Alzheimers Dement. 2016, 12:459-509. 10.1016/j.jalz.2016.03.001

71. Kumar A, Sidhu J, Goyal A, Tsao JW: Alzheimer disease . StatPearls [Internet]. StatPearls Publishing, Treasure Island, FL; 2023.

72. Helaly HA, Badawy M, Haikal AY: Deep learning approach for early detection of Alzheimer's disease . Cognit Comput. 2022, 14:1711-27. 10.1007/s12559-021-09946-2

73. Winblad B, Wimo A, Wetterholm A-L, et al.: P.4.044 Long-term efficacy of donepezil in patients with mild to moderate Alzheimer's disease: results from a one-year placebo-controlled study and two-year follow-up study. Eur Neuropsychopharmacol. 2003, 13: 10.1016/S0924-977X(03)92238-3

74. Winblad B, Engedal K, Soininen H, et al.: A 1-year, randomized, placebo-controlled study of donepezil in patients with mild to moderate AD. Neurology. 2001, 57:489-95. 10.1212/wnl.57.3.489

75. Winblad B, Brodaty H, Gauthier S, et al.: Pharmacotherapy of Alzheimer's disease: is there a need to redefine treatment success?. Int J Geriatr Psychiatry. 2001, 16:653-66. 10.1002/gps.496

76. Whitehead A, Perdomo C, Pratt RD, Birks J, Wilcock GK, Evans JG: Donepezil for the symptomatic treatment of patients with mild to moderate Alzheimer's disease: a meta-analysis of individual patient data from randomised controlled trials. Int J Geriatr Psychiatry. 2004, 19:624-33. 10.1002/gps.1133

77. Farlow M, Anand R, Messina J Jr, Hartman R, Veach J: A 52-week study of the efficacy of rivastigmine in patients with mild to moderately severe Alzheimer's disease. Eur Neurol. 2000, 44:236-41. 10.1159/000008243

78. Chu LW: Alzheimer's disease: early diagnosis and treatment . Hong Kong Med J. 2012, 18:228-37.

79. Puppala GK, Gorthi SP, Chandran V, Gundabolu G: Frontotemporal dementia - current concepts. Neurol India. 2021, 69:1144-52. 10.4103/0028-3886.329593

80. Battineni G, Chintalapudi N, Hossain MA, et al.: Artificial intelligence models in the diagnosis of adult-onset dementia disorders: a review. Bioengineering (Basel). 2022, 9: 10.3390/bioengineering9080370

81. Tsai RM, Boxer AL: Treatment of frontotemporal dementia . Curr Treat Options Neurol. 2014, 16: 10.1007/s11940-014-0319-0

82. Liepelt I, Gaenslen A, Godau J, Di Santo A, Schweitzer KJ, Gasser T, Berg D: Rivastigmine for the treatment of dementia in patients with progressive supranuclear palsy: clinical observations as a basis for power calculations and safety analysis. Alzheimers Dement. 2010, 6:70-4. 10.1016/j.jalz.2009.04.1231

83. Litvan I, Phipps M, Pharr VL, Hallett M, Grafman J, Salazar A: Randomized placebo-controlled trial of donepezil in patients with progressive supranuclear palsy. Neurology. 2001, 57:467-73. 10.1212/wnl.57.3.467

84. Fabbrini G, Barbanti P, Bonifati V, Colosimo C, Gasparini M, Vanacore N, Meco G: Donepezil in the treatment of progressive supranuclear palsy. Acta Neurol Scand. 2001, 103:123-5. 10.1034/j.1600-0404.2001.103002123.x

85. Litvan I, Gomez C, Atack JR, Gillespie M, Kask AM, Mouradian MM, Chase TN: Physostigmine treatment of progressive supranuclear palsy. Ann Neurol. 1989, 26:404-7. 10.1002/ana.410260318

86. Kimura T, Takamatsu J: Pilot study of pharmacological treatment for frontotemporal dementia: risk of donepezil treatment for behavioral and psychological symptoms. Geriatr Gerontol Int. 2013, 13:506-7. 10.1111/j.1447-0594.2012.00956.x

87. Mendez MF, Shapira JS, McMurtray A, Licht E: Preliminary findings: behavioral worsening on donepezil in patients with frontotemporal dementia. Am J Geriatr Psychiatry. 2007, 15:84-7. 10.1097/01.JGP.0000231744.69631.33

88. Kertesz A, Morlog D, Light M, Blair M, Davidson W, Jesso S, Brashear R: Galantamine in frontotemporal dementia and primary progressive aphasia. Dement Geriatr Cogn Disord. 2008, 25:178-85. 10.1159/000113034

89. Moretti R, Torre P, Antonello RM, Cattaruzza T, Cazzato G, Bava A: Rivastigmine in frontotemporal dementia: an open-label study. Drugs Aging. 2004, 21:931-7. 10.2165/00002512-200421140-00003

90. Zafar S, Yaddanapudi SS: Parkinson disease. StatPearls [Internet]. StatPearls Publishing, Treasure Island, FL; 2023.

91. Alexoudi A, Alexoudi I, Gatzonis S: Parkinson's disease pathogenesis, evolution and alternative pathways: a review. Rev Neurol (Paris). 2018, 174:699-704. 10.1016/j.neurol.2017.12.003

92. Iida M, Miyazaki I, Tanaka K, Kabuto H, Iwata-Ichikawa E, Ogawa N: Dopamine D2 receptor-mediated antioxidant and neuroprotective effects of ropinirole, a dopamine agonist. Brain Res. 1999, 838:51-9. 10.1016/s0006-8993(99)01688-1

93. Scheller D, Stichel-Gunkel C, Lübbert H, Porras G, Ravenscroft P, Hill M, Bezard E: Neuroprotective effects of rotigotine in the acute MPTP-lesioned mouse model of Parkinson's disease. Neurosci Lett. 2008, 432:30-4. 10.1016/j.neulet.2007.12.001

94. Li C, Guo Y, Xie W, Li X, Janokovic J, Le W: Neuroprotection of pramipexole in UPS impairment induced animal model of Parkinson's disease. Neurochem Res. 2010, 35:1546-56. 10.1007/s11064-010-0214-3

95. Olanow CW, Hauser RA, Jankovic J, et al.: A randomized, double-blind, placebo-controlled, delayed start study to assess rasagiline as a disease modifying therapy in Parkinson's disease (the ADAGIO study): rationale, design, and baseline characteristics. Mov Disord. 2008, 23:2194-201. 10.1002/mds.22218

96. Li BD, Bi ZY, Liu JF, Si WJ, Shi QQ, Xue LP, Bai J: Adverse effects produced by different drugs used in the treatment of Parkinson's disease: a mixed treatment comparison. CNS Neurosci Ther. 2017, 23:827-42. 10.1111/cns.12727

97. Chou KL: Adverse events from the treatment of Parkinson's disease . Neurol Clin. 2008, 26:S65-83. 10.1016/j.ncl.2008.05.003

98. Murman DL: Early treatment of Parkinson's disease: opportunities for managed care . Am J Manag Care. 2012, 18:S183-8.

99. Chin KS, Teodorczuk A, Watson R: Dementia with Lewy bodies: challenges in the diagnosis and

2023 Mohamed et al. Cureus 15(10): e47004. DOI 10.7759/cureus.47004

8 of 9

management. Aust N Z J Psychiatry. 2019, 53:291-303. 10.1177/0004867419835029

100. Galvin JE, Chrisphonte S, Cohen I, et al.: Characterization of dementia with Lewy bodies (DLB) and mild cognitive impairment using the Lewy body dementia module (LBD-MOD). Alzheimers Dement. 2021, 17:1675-86. 10.1002/alz.12334

101. Tampi RR, Young JJ, Tampi D: Behavioral symptomatology and psychopharmacology of Lewy body dementia. Handb Clin Neurol. 2019, 165:59-70. 10.1016/B978-0-444-64012-3.00005-8

102. Watts KE, Storr NJ, Barr PG, Rajkumar AP: Systematic review of pharmacological interventions for people with Lewy body dementia. Aging Ment Health. 2023, 27:203-16. 10.1080/13607863.2022.2032601

103. Vanhaute H, Persoons P: Early use of memantine in the treatment of Lewy body dementia. [Article in Dutch]. Tijdschr Psychiatr. 2016, 58:814-7.