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COMPARISON AND ANALYSIS OF THE USE OF ADVANCED METHODS OF ARTIFICIAL INTELLIGENCE FOR NEURODEGENERATIVE DISEASES

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Abstract:

The paper deals with the comparison of existing methods of using artificial intelligence (AI) for the effective diagnosis of selected neurodegenerative diseases. The use of AI for disease diagnosis has advanced significantly in the last decade, as well as the use of various machine learning methods of speech recognition for disease diagnosis. The use of new technologies based on AI can help find a solution to a non-invasive, easy-to-apply method for detection and subsequent treatment of brain diseases. Diagnosis of neurodegenerative diseases has mainly been performed using neuroimaging methods such as magnetic resonance imaging or positron emission tomography or single-photon emission computed tomography. The aim was to analyse existing AI-assisted diagnostic approaches based on peer-reviewed publications and to highlight current trends in the diagnosis of Alzheimer's and Parkinson's diseases. Finally, we showed our approach to early diagnosis of neurodegenerative diseases.

Keywords:

Neurodegenerative diseases, Alzheimer's disease, Parkinson's disease, spontaneous speech, artificial intelligence, machine learning, deep learning.

ACM Computing Classification System:

Machine learning algorithms, machine translation, natural language generation, speech recognition, lexical semantics, phonology.

Introduction

The most common neurodegenerative diseases are Alzheimer's disease (AD), Parkinson's disease (PD) and others, which are often determined by neurological and psychiatric examination using a variety of ancillary tests such as magnetic resonance imaging (MRI), positron emission tomography (PET), speech and vision tests or laboratory tests of cerebrospinal fluid (CSF) or blood. In this article, we focus on two neurodegenerative diseases in particular: AD, including the Mild Cognitive Impairment stage (MCI), and PD.

Around 35 million people worldwide live with AD or another dementia. By 2030, the number is expected to exceed 65 million. Alzheimer's disease and other forms of dementia are currently among the 10 most common causes of death worldwide, with the 3rd most common deaths in Europe and the United States in 2019 [1].

The number of patients with neurodegenerative diseases in the world is increasing every year, similarly in Slovakia, according to the data of the National Centre of Health Information in Slovakia there are more than 40 thousand of them and according to the latest surveys it is up to twice as many [2].

1 Current Research on Neurodegenerative Diseases

The goal of our Early Warning of Alzheimer's (EWA) project is to develop a data collection methodology, select appropriate images, videos, questions and procedures to collect input data for early diagnosis of AD, MCI and PD, especially using speech recognition. As part of the EWA project, we analysed publications on neurodegenerative diseases and developed a research review until 2020. Authors Boschi and colleagues analysed the speech of people with neurodegenerative diseases [3]. They performed a systematic analysis of 61 publications focusing on language variables extracted from patients' speech up to 2017. In their analysis of spontaneous speech, they investigated the phonetic, phonological, lexical-semantic, morphosyntactic and pragmatic levels of language, for which they defined different characteristic linguistic variables. Their conclusions are as follows: Alzheimer's disease is most pronounced at the lexico-semantic (80%), discourse-pragmatic (77%), syntactic (57%) and phonetic (55%) levels. In patients' speech, it manifests itself at the semantic level by word finding, word correction and repetition [4]. At the phonetic level, the speech of AD patients is mainly characterized by low frequency of speech and frequent hesitations [5]. When comparing amnestic mild cognitive impairment (aMCI) and AD, aMCI patients were found to use a greater number of correct nouns instead of pronouns than Alzheimer's patients. Similarly, aMCI patients' interviews appear to be more effective, coherent, and informative than Alzheimer's patients' interviews.

Parkinson's disease (PD) is often associated with motor speech impairment that affects phonation, articulation, resonance, and prosody [6], detected mainly by variables related to pause duration [7] and change in prosody [8]. Language deficits include morpho-syntactic processing, especially verb generation [9]. An important summary of the results for AD, aMCI and PD is shown in Table 1, Table 2 and Table 3 adapted from [3], where aMCI is the amnestic MCI and abbreviation SD means standard deviation.

Table 1. Relevant linguistic features for AD, aMCI and PD versus Healthy Controls (HC).

Linguistic level	**Linguistic feature**	**AD vs. HC**	**aMCI vs. HC**	**PD vs. HC**
Phonetic and	Speech rate	AD < HC	-	not rel.
Phonological	Number of pauses	-	-	PD > HC
	Between–utterance pause duration	-	-	PD > HC
	Prosody: F0 SD	not rel.	-	PD < HC
	Prosody: Intensity SD	-	-	PD < HC
	Hesitation ratio	AD > HC	-	-
Lexicosemantic	Pronoun-noun ratio	AD > HC	-	-
	Closed-class words	AD > HC	not rel.	not rel.
	Idea density	AD < HC	-	-
	Frequency	AD > HC	-	-
	Semantic errors	AD > HC	-	-
	Word-finding difficulties	AD > HC	-	-
	Indefinite terms	AD > HC	-	-

Table 2. Relevant linguistic features for AD versus HC and for PD versus HC.

Linguistic level	Linguistic feature	AD vs. HC	PD vs. HC
Morphosyntactic	Inflectional errors	AD > HC	not rel.
Syntactic	Mean length of utterances	AD < HC	not rel.
	Reduced sentences	AD > HC	-
Discourse	Discourse markers	AD > HC	-
and	Cohesion	AD < HC	-
Pragmatic	Correct pronoun	AD < HC	-
	Local coherence	AD < HC	not rel.
	Global coherence	AD < HC	not rel.

Table 3. Comparison between Alzheimer's disease and amnestic Mild Cognitive Impairment.

Linguistic level	Linguistic feature	AD vs. aMCI
Lexico-semantic features	Pronoun rate	AD > aMCI
	Idea density	AD < aMCI
Discourse and pragmatic	Information content	AD < aMCI
features	Index of discourse effectiveness	AD < aMCI
	Efficiency	AD < aMCI

2 Alzheimer's Disease

We searched the SCOPUS database for review publications for Alzheimer's disease [10], [11]. Until 1984, the diagnosis of patients with AD was almost entirely based on clinical examination [10], mainly using the Mini Mental State Examination (MMSE) or the Montreal Cognitive Assessment (MoCA). At present, magnetic resonance imaging (MRI) and positron emission tomography (PET) have led to a broader understanding of neuropathological processes. In addition to expensive neuroimaging and detailed medical examination, there is an invasive analysis of cerebrospinal fluid (CSF) [12]. However, cheaper other approaches are being sought, such as blood biomarkers and spontaneous speech analysis using artificial intelligence. No blood biomarker has yet achieved sufficient accuracy [13].

In the analysis of spontaneous speech, prosody is most often studied in people with neurodegenerative diseases because it relates to the phonetic and phonological properties of speech. Specifically, it involves the analysis of speech rhythm along with other parameters related to temporal and acoustic measures of voice, such as articulatory rhythm, vocal intensity (analysis of loudness and changes in amplitude over time), timing and frequency (changes in acoustic signal frequencies, colour or shape structure). There are several studies that jointly evaluate the process of extracting features from the vocal signal using different vocal parameters and different qualifiers [10].

For the analysis of spontaneous speech and sound, the following Table 4 lists the common properties used to describe the acoustic characteristics of the voice used to detect AD [11]. We use abbreviation F0: Fundamental Frequency, SD: Standard Deviation, VR: Variation Range.

Table 4. Main conventional features used in Alzheimer's disease.

<table>
<tr><td rowspan="5">Phonetic aspects</td><td rowspan="3">Interruptions</td><td>Percentage and number of pauses of voice,
Percentage without voice</td></tr>
<tr><td>Number and percentage of voice breaks</td></tr>
<tr><td>(MEAN, MAX, MIN)</td></tr>
<tr><td rowspan="2">Voice periods</td><td>Number of pulses analysed as voice</td></tr>
<tr><td>Period (MEAN, SD)</td></tr>
<tr><td rowspan="5">Frequential Aspects</td><td rowspan="4">Fundamental frequency and spectrum</td><td>F0 (MEAN, MAX, MIN, SD, VR)</td></tr>
<tr><td>Short time energy or spectral centroid</td></tr>
<tr><td>High and low global pitch</td></tr>
<tr><td>Autocorrelation</td></tr>
<tr><td>Fluctuations</td><td>Jitter (Short term, cycle-to-cycle, perturbations in the F0): local jitter, local absolute jitter, relative average perturbation jitter</td></tr>
<tr><td rowspan="5">Intensity</td><td rowspan="4">Amplitude</td><td>Intensity of voice and unvoiced signals (SD, MAX, MIN)</td></tr>
<tr><td>Square Energy Operator (SD)</td></tr>
<tr><td>Teager-Kaiser Energy Operator (SD)</td></tr>
<tr><td>Root Mean Square Amplitude</td></tr>
<tr><td>Phonatory stability</td><td>Period perturbation, shimmer (short term, cycle-to-cycle, perturbations in the amplitude of the voice): local shimmer, amplitude perturbation quotient</td></tr>
<tr><td rowspan="2">Voice Quality</td><td rowspan="2">Noise</td><td>Harmonic-to-Noise Ratio</td></tr>
<tr><td>Noise-to-Harmonic Ratio</td></tr>
</table>

Machine learning (ML) and Deep learning (DL) techniques are used for several of the above methods of detecting neurodegenerative disease. The most used methods for machine learning are support vector machines, decision trees, k-nearest neighbours, linear regression, linear discriminant analysis, neural networks, Bayesian networks and also techniques by combining several models such as bootstrap aggregating, boosting, stacking detailed [14].

To evaluate machine learning models, accuracy is most often used according to the relationship:

$$\text{Accuracy} = (TP + TN) / (TP + TN + FP + FN)$$

where the values are TP - true positive, TN - true negative, FP - false positive and FN - false negative classifications.

Sensitivity (also recall) and specificity (also TNR) values are often given:

$$\text{Sensitivity} = TP / (TP + FN)$$
$$\text{Specificity} = TN / (TN + FP)$$

The average accuracy of AD disease classification reported in the analysed publications was 80%, with the average number of patients being 37 [11]. The following (Tab.5) lists the publications where the accuracy was greater than 90%. The acronym ANN stands for artificial neural network, CNN stands for convolutional neural network and NHR means noise-to-harmonics ratio.

Table 5. Predictive studies on early diagnosis of Alzheimer's disease.

References	Year	Sample	Parameters	Predictive value	Analysis method
López-de-Ipiña et al. [15]	2013	HC (20), AD (20)	Combination of two feature sets: emotional speech analysis (acoustic, voice quality, and duration features) and emotional temperature (prosodic and paralinguistic features)	AD: 75.2-97.7%	ANN
López-de-Ipiña et al. [16]	2015	HC (20), AD (20)	Automatic selection of spontaneous speech features and of maximum, minimum, variance, standard deviation, median, and mode average for full signal and voiced signal	AD: 87.30-92.43%	ML
Nasrolahzadeh et al. [17]	2018	HC (30), AD (30)	Higher-order spectral analysis	AD: 94.18-97.71%	ML
König et al. [18]	2018	MCI (44), AD (27)	Different combination of features extracted for every comparison	MCI vs. AD = 92%,	ML
López-de-Ipiña et al. [19]	2018	HC (187), MCI (38)	Several types of features are used to model both linear and non-linear disfluencies and speech. A total of 920 features are obtained. The best results are achieved with the 25-feature set.	MCI: 92-95%	DL - CNN
Martínez-Sánchez et al. [20]	2018	HC (98), AD (47)	Age, minimum amplitude, maximum amplitude difference, mean and standard deviation of the NHR; asymmetry; standard deviation in the first formant; formant 3 bandwidth; standard deviation of the Acoustic Voice Quality Index; tone variability; Normalized Pairwise Variability Index	AD: 92.4%	DA

In the last two publications, there are a larger number of patients in whom they achieved results better than 90%. For AD patients, better classification accuracy was achieved by discriminant analysis (DA) of 92% in a study [20], which analysed the speech of 47 AD patients with a healthy group of 98 people. They selected the following characteristics for machine learning: age, minimum amplitude, maximum amplitude difference, mean and standard deviation, NHR; asymmetry; standard deviation in the first formant; bandwidth of formant 3; standard deviation of acoustic voice quality index; tone variability; normalized index of pair variability. To classify MCI diseases, they implemented the deep learning method with an accuracy of 92% [19]. They compared speech characteristics from 38 AD patients and a healthy control group of 187 people. They obtained 920 functions for the analysis of modelling linear and nonlinear disfluencies and speech, and by choosing 25 functions they achieved the best results.

They performed the classification using the CNN method, using conventional linear elements, as well as the Castiglioni fractal dimension and the Multiscale Permutation Entropy. They concluded that the choice of property was best using the nonparametric Mann-Whitney U-test.

For the analysis of machine learning, the authors stated in the study [10] that the results using SPECT (Single-photon emission computed tomography), PET (Positron Emission Tomography), and MRI devices are better, but they are extremely expensive and can only be performed by specialized workplaces. Speech signal analysis is cheaper and can also be performed on mobile phones. Therefore, the best approach today seems to be to perform multiple tasks and select different functions to combine into a more powerful resulting algorithm.

3 Parkinson's Disease

In the SCOPUS database, we identified review publications on Parkinson's disease [21]. The authors extracted the studies using inclusion and exclusion criteria from the PubMed and IEEEXplore databases for Parkinson's disease. A total of 209 studies focusing on PD and machine learning were analysed by February 2020. The studies were divided into methodological and clinical, and according to the method of scanning and the type of device, respectively.

In Table 6, the columns list the methods of voice, gait, hand, MRI, SPECT, PET, and CSF examinations, and the rows of the table list the numbers out of a total of 209 studies that focused on methodological studies or clinical trials, and the other two rows list the average precision of the listed methods of these studies and their standard deviation (SD). The abbreviations are SPECT: single photon emission computed tomography, PET: positron emission tomography, CSF: cerebrospinal fluid, Combo: combination of methods.

Table 6. Overview of the number of studies according to the method of scanning the device type.

	Voice	**Gait**	**Hand**	**MRI**	**SPECT**	**PET**	**CSF**	**other**	**Combo**
Methodology	51	35	12	15	2	3	0	4	10
Clinical	4	16	4	21	12	1	5	6	8
Average	91,1	89,0	87,3	88,1	94,5	85,6	50,0	91,9	92,8
SD	8,5	8,5	6,4	7,7	4,2	6,8	0,0	6,4	5,9

The total number of methodological studies was 134 and their average patient sample size was 137, in contrast the number of clinical studies was only 72 but the average patient sample size was larger at 266. In the methodological studies, voice recordings were the most commonly used data modality (n = 51), followed by GAIT motion (n = 35) and then MRI data (n = 15). For clinical studies, MRI data were important (n = 21), followed by GAIT (n = 16) and then SPECT (n = 12) . The average accuracy achieved across studies for each data type was highest for SPECT (94.5%) and a combination of multiple methods (92.8%) and voice recording (91.1%). The following Figure 1 shows the average accuracy for the defined modalities and their standard deviations in the reported studies.

In terms of the frequency of use of machine learning methods in selected PD studies, Mei et al. [21] divided these methods into the following types: SVM, support vector machine; NN, neural network; EL, ensemble learning; k-NN, nearest neighbour; regr, regression; DT, decision tree; NB, naive Bayes; DA, discriminant analysis; other, data/models. Figure 2 shows the percentage of machine learning methods used for Voice, Gait and Hand adopted from [21].

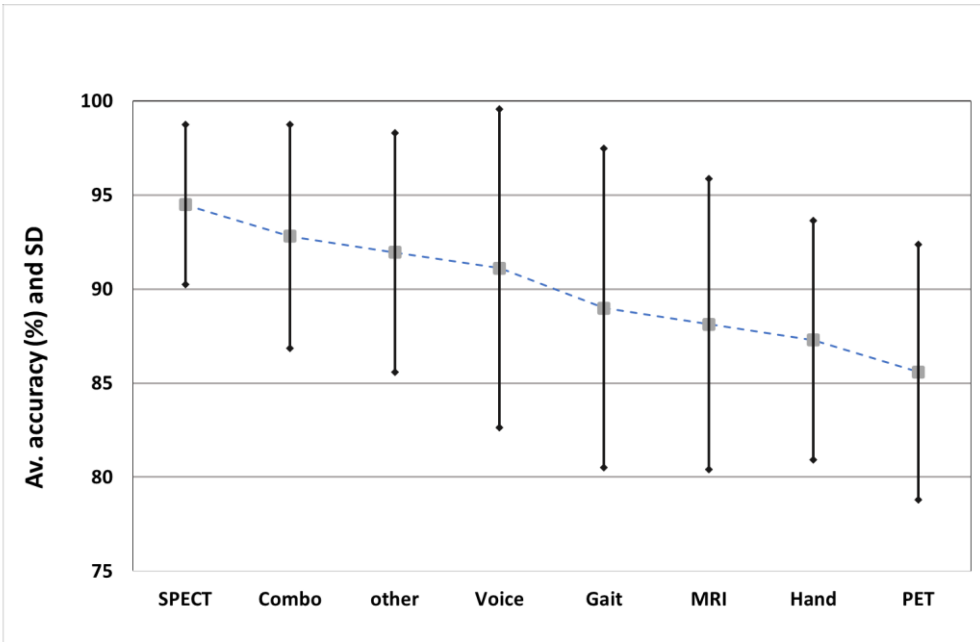

Figure 1. Average accuracy for a given modality with standard deviation for selected studies reported in [21].

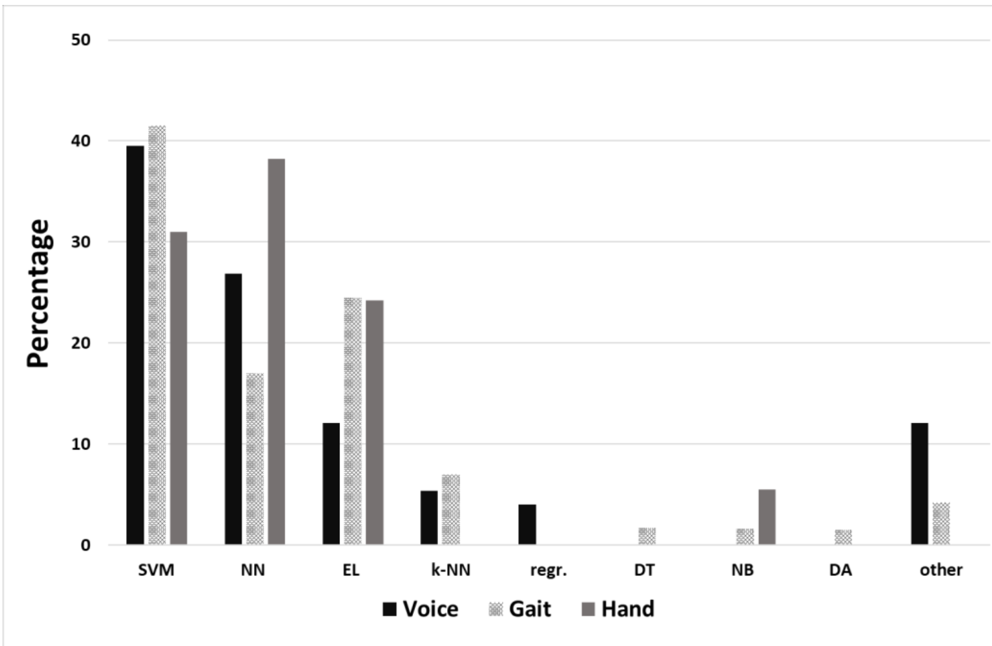

Figure 2. Frequency of machine learning methods for Voice, Gait, and Hand.

Some studies for the Hand measured mobile phone movement in patients with PD. The resulting machine learning qualifiers using neural networks achieved 95% accuracy (see Figure 2). These results suggest that the mobile phone accelerometer can accurately detect vibrational motion in PD patients.

The following Table 7 selects publications from the Voice dataset (n = 55) in which the number of patients with PD was at least 40 and the accuracy or one of the sensitivity and accuracy values was greater than 90% [21].

Table 7. Publications according to criteria: number of PD > 40 a (Accuracy or Sensitivity or Precision) > 90%

References	**Year**	**Sample**	**Analysis method**	**Predictive value**
Erdogdu Sakar et al. [22]	2017	PD(42) + HC(8)	KNN, SVM, ELM witha train-validation ratio of 70:30	Accuracy = 96,4%
Sztaho et al. [23]	2019	PD(55) + HC(33)	KNN, SVM-linear, SVM-RBF, ANN, DNN with leave-one-subject-out cross validation	Accuracy = 89,3% Sensitivity = 90,2%
Tracy et al. [24]	2019	PD(246) + HC(2023)	regression, random forest, gradient boosted decision trees with 5-fold cross validation	Precision = 90,1%
Wodzinski et al. [25]	2019	PD(50) + HC(50)	ResNet with train-validation ratio of 90:10	Accuracy = 91,7% Precision = 92,0%
Yaman et al. [26]	2020	PD(40) + HC(40)	KNN, SVM with 10-fold cross	Accuracy = 91,3% Precision = 91,3%

4 Discussion

The Early Warning of Alzheimer (EWA) project is concerned with the early detection of Alzheimer's and Parkinson's diseases [27]. The project is implemented by researchers from AXON PRO, the Institute of Informatics of the Slovak Academy of Sciences and the Faculty of Informatics of the Pan-European University together with doctors from the Faculty of Medicine of the P. J. Šafárik University. Within the framework of the project, a mobile application for automatic detection was developed for the collection of speech data of healthy people and patients with neurodegenerative diseases for automatic detection of AD and PD with some accuracy. The speech recording system was designed using image naming and verbal description of images being similar to the well-known picture "Cookie Theft" (new version Stealing Cookies in [28]). In the following, we briefly describe the process of acquiring the data needed to best predict AD and PD.

According to the proposed procedure, patients diagnosed with AD and PD are closely monitored for how they respond to the displayed pictures, and their spontaneous speech is recorded either at the MEMORY Centre for AD or at the Neurology clinic for PD. In the case of diagnosed patients, all available information in addition to medical history is used to make an accurate diagnosis. Three selected psychological tests are also administered: the Montreal Cognitive Assessment (MoCA), the Beck Depression Inventory (BDI), and the Generalized Anxiety Disorder (GAD-7). According to the above scenario, audio recordings of picture descriptions as well as the MoCA, BDI, and GAD-7 tests are also recorded for a healthy control of the population.

The audio recordings were processed using specialized software and a suitable feature selection algorithm for speech and sound processing, which was developed at the Institute of Informatics of the Slovak Academy of Sciences in Bratislava. Preliminary experiments indicate that recordings of patients' spontaneous speech in Slovak while describing pictures using a mobile app may also reveal subtle changes in the voice of people with neurodegenerative diseases, which will help in early detection of AD and PD.

As can be seen from the tables presented in the previous sections of this paper, many of the machine learning applications in the reviewed papers relied on relatively small amounts of collected data. Obtaining data from a large group of clinical trial participants is critical for the most accurate predictions, which is what we are trying to accomplish in our EWA project. Data collected from Alzheimer's and Parkinson's patients and a group of healthy people are evaluated using special artificial intelligence algorithms to best determine accuracy, sensitivity, and specificity.

Conclusion

Patients with suspected Alzheimer's and Parkinson's disease need to be identified as early as possible so that treatment can be started early, and the patient's disease progresses as little as possible. Results up to date show that the detection of neurodegenerative diseases using automated analysis of human voice and speech can be achieved with an accuracy of more than 90% under laboratory conditions. As we showed in Table 7, the sensitivity of disease prediction can reach more than 90% depending on the selected group of patients and healthy people, the processing of spontaneous speech of this group, and finally the algorithms and methods of artificial intelligence.

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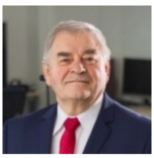

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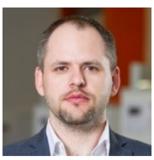

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