NEW TECHNOLOGIES IN THE PREVENTION OF NEURODEGENERATIVE DISEASES.

Queiroz A V§; Ishioca E R§; Svizzero FC§; DelMonaco ADM§.

§ University Center of Americas, São Paulo, Brazil.

Abstract. The article refers to new technologies for the prevention of neurodegenerative diseases and aims to show their importance and their contribution to the health area, developing new exam models for early diagnosis of diseases such as Parkinson's and Alzheimer's. Academic articles and articles from websites and magazines pieces were used as a basis for the construction of this article, highlighting new diagnostic methods based on the use of platinum electrodes, blood biomarkers and Artificial Intelligence, which meet the need of the health system, as they are viable, innovative and practical, both for professionals and patients, saving their time and consequently improving their quality of life, when available to the population.

Keywords. Neurodegenerative Disease. Early Diagnosis. Parkinson's Disease. Alzheimer. Artificial Intelligence.

Introduction. Just like the improvement of the technology and new discoveries, the Preventive Medicine has been evolving progressively to the benefit of patients and doctors. The creation of new technologies to the health area are not aimed only to the development of more efficient treatments to diseases, but also to provide new ways to prevent them. Doing preventive exams, one may continue healthy and willing to have a better quality of life.

Nowadays, one of the biggest difficulties to the scientific community is providing early and accurate diagnosis to neurodegenerative diseases. The complexity of comprehension and understanding of the molecular mechanisms that are subjected to the neuronal degeneration is understood as a great challenge to the development of some tools to perform an early diagnosis as well as to do an efficient treatment of these diseases. (SUMMIT SAÚDE, 2020).

The available tests to identify neurodegenerative diseases, which involve some psychic and behavior evaluations, as well as blood and image exams, do not allow an early prevention, nor a precise one. As a consequence, researchers and scientists try to develop techniques that use biomarkers (disease development probability index). (ALVES, 2020).

Just like the majority of things, the diagnosis methods will evolve as the years go by. One example is the Artificial Intelligence, that will be connected to the medical field in the future, providing precise diagnosis, identifying diseases before they manifest and increasing the patients' quality of life. (EQUIPE VERITÀ, 2019).

It's important to point out, however, that a technology like the AI will not replace the health professionals, since its purpose is assisting doctors in their jobs when providing the patients' well-being.

In this article, we present the impact and contribution that the evolution of technology generates to the health field, more precisely to the Preventive Medicine, when it comes to neurodegenerative diseases.

Showing how this technological evolution has been key in the development of new exam models that aim to the early diagnosis of neurodegenerative diseases and analising the proportion of the impact caused by identifying diseases in their early stages or even before they show up, to begin the treatment as soon as possible.

"Neurodegenerative Disease" is a term used to define diseases that affect the human brain, crushing neurons in an irreversible way. Diseases with these characteristics usually manifest in elder people.

Neurons are the pillars of the nervous system, and they're responsible for the nervous impulses transmission. However, they don't have the capacity to reproduce themselves and can't be replaced either, which means they're finite. (SUPERA, 2020).
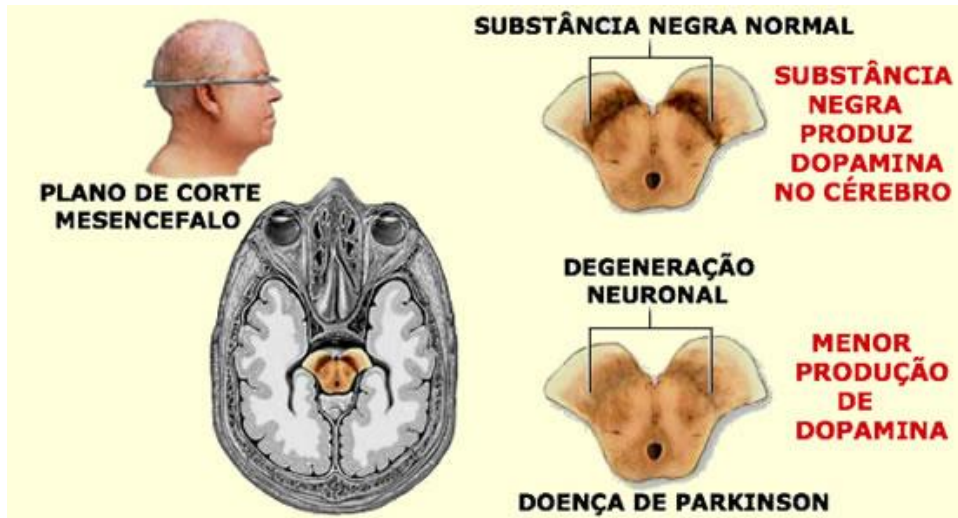
Considering these aspects, neurodegenerative diseases become irreversible. Throughout the years, the disease reveals itself more and more debilitating, as it kills the neurons and cause some motor problems (lack of coordination), mental problems (dementia) to the patient, harming their life quality and well as their families'.

The *Alzheimer* and Parkinson's disease are examples of neurodegenerative diseases.
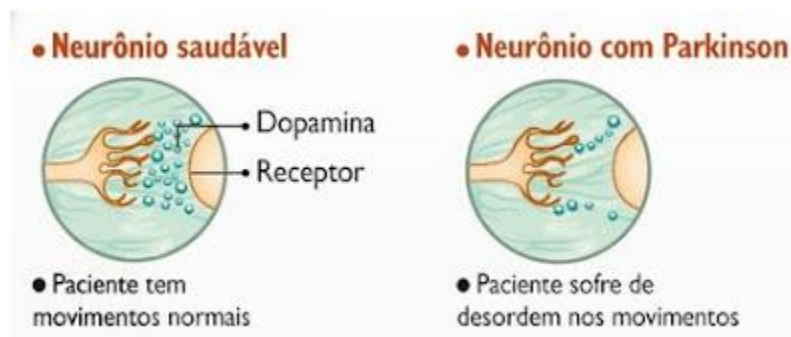
Parkinson's disease

It's a result from the nervous system's degeneration, more specific, from a part of the brain called basal ganglia. This degeneration causes a smaller dopamine production and consequently, a decrease in the number of connections between the cells in the area (SILVA, 2017). The dopamine is responsible for helping the motor coordination and its lack might result in shakings, muscular rigidity and a bigger difficulty to perform some voluntary movements.

Image 1 – The degeneration of the neurons in this region is the disease's main cause.

Source:https://portal.unisepe.com.br/asmec/wpcontent/uploads/sites/10006/2018/10/ENF ERMAGEM-24.pdf

Image 2 – The dopamine low concentration causes a unmanageability when transmitting nervous impulses.

Source:https://portal.unisepe.com.br/asmec/wpcontent/uploads/sites/10006/2018/10/ENF ERMAGEM-24.pdf

According to WHO (2018), 1% of the world population above 65 years old had *Parkinson's disease*. The estimate for Brazil is that more than 200.000 people have it. (G1 SÃO CARLOS E ARARAQUARA, 2020).

Although there's no cure for the disease, there are treatments that combine medicine with physical therapy, occupational therapy, psychotherapy and speech therapy.

Parkinson's disease early diagnosis

Diagnosing the PD early is quite important so the treatment can begin as soon as possible, in which is highly recommended a neurologist's follow-up. The PD is usually diagnosed through pre-stablished clinical criteria, being confirmed if the patient presents at least three symptoms and the doctor discards other diseases that also damage the Nervous System. Besides these, there are some image exams, such as magnetic resonance, positron emission tomography and single photon emission computed tomography, which are essential to a more precise diagnosis, considering their capacity to prove morphological damage to the nervous system (SILVA, 2017).

Researchers from the Universidade Federal de São Carlos (UFSCar) have created an equipment able to early identify the PD through two bio-markers verification – both exist in the organism. Aiming to detect the disease in its early stage, the researchers developed flexible platinum electrodes, used to observe two bio-markers: the dopamine and the protein DJ-1, both directly connected to the DP. (G1 SÃO CARLOS E ARARAQUARA, 2020). (Our translation)

Image 3 – Flexible platinum electrodes used as electrochemical bio-sensors to determine biomarkers related to the *Parkinson Disease*.
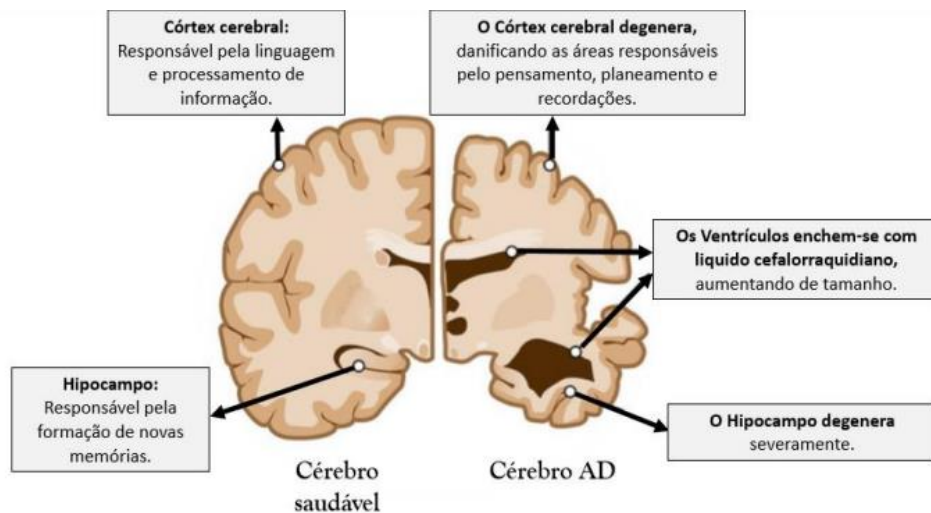

Source: https://g1.globo.com/sp/sao-carlos-regiao/noticia/2020/09/23/pesquisadores-da-ufscar-desenvolvem-equipamento-para-deteccao-precoce-de-parkinson.ghtml

The idea of these bio-markers usage is helping the DP early diagnosis, considering that if discovered early, the patient may go through a more efficient treatment, slowing down some symptoms and damage to the nervous system.

Alzheimer

Alzheimer's, a neurodegenerative disease, is known to damage and destroy brain cells, ultimately atrophying cognitive functions. In its early stage, the disease causes recent memory loss, while at a more advanced stage, it affects the patient's ability to spatially orient, understand momentary situations and even communicate. (SUPERA, 2020). (Our translation)

Image 4 – Main diferences between a healthy brain ando ne with *Alzheimer*.

Source: https://sapientia.ualg.pt/bitstream/10400.1/10408/1/Tese.pdf

As the patient's condition worsens, he becomes increasingly dependent on his family, even for common daily activities, such as taking a shower or preparing meals. Occasions like these are what highlight Alzheimer's as one of the most debilitating neurodegenerative diseases.
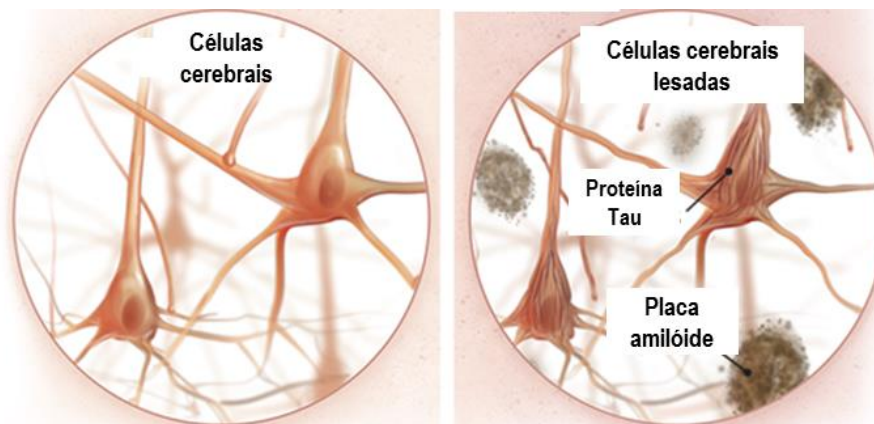
Currently, no cure for the disease has been found, but through combined treatments of drugs and therapies, it is possible to repress the patient's symptoms and delay the progression of the case.

Early Alzheimer's diagnosis by blood test

Researchers from the United States and Sweden conducted studies and formulated a blood test, which showed the ability to calculate the amount of a specific protein in the body, called p-tau217, and thus detect, in advance, the manifestation of Alzheimer's disease up to 20 years, or still in its early stages. (ALVES, 2020). (Our translation)

Through the exam, it is possible to observe the levels of beta-amyloid present in the blood and, according to its rate, if it presents a level very different from normal, point out the accumulation of protein in the brain, which is a very characteristic aspect of the disease.

Image 5 – Alteration of tau protein and beta-amyloid levels in an Alzheimer's brain

Source: http://www.ineuro.com.br/para-os-pacientes/alzheimer-reconhecendo-seus-sintomas/

Adding the altered rate of this protein in the blood with the genetic variant APOE4 and the patient's advanced age, it is possible to confirm Alzheimer's with an accuracy of up to 94%, in a simple, cheap and yet efficient way, without the need to perform a tomography PET scan to quantize, by imaging, beta-amyloid levels in the brain, saving cost and time. (ALVES, 2020).

Early Alzheimer's diagnosis by eye exam

It was pointed out by scientists that, based on a very common eye exam, an angiography by optical coherence tomography, there is the possibility of detecting Alzheimer's in people with the disease, but who have not yet had any symptoms manifested, given the observation of that people with Alzheimer's exhibit visible changes in the central region of their retinas and in their optic nerves. (UFJF NOTÍCIAS, 2015).

It is common for all people for the center of the eye retina to have a region where there are no blood vessels. However, interestingly, patients with Alzheimer's have a significant growth of this specific region of the retina and, being an alteration that is not found in people who do not have high levels of beta-amyloid in the brain, it becomes an indicator of great importance for early diagnosis of the disease.

Artificial Intelligence in the early diagnosis of neurodegenerative diseases

According to a survey carried out by the Institute of Neuroscience at the University of Sheffield and published in the journal Nature Reviews Neurology, it was found that the use of Artificial Intelligence (AI), incorporated into the health area and used daily, can help to reduce the social and economic impact, caused by neurodegenerative diseases. (SUMMIT SAÚDE, 2020). (Our translation)

The study exemplifies how AI technologies operate, based on machine learning algorithms, which have the ability to detect neurodegenerative diseases in their early stages, in addition to constantly collecting data for later use in making increasingly accurate diagnoses. Thus, patients would be diagnosed early, without the need to carry out many tests, resulting in more effective treatments for patients and cost cuts for the health system.

In the future, neurodegenerative diseases may even be diagnosed by AI, exclusively, by analyzing how a person pronounces certain words, or how he writes them. (PEBMED, 2018). Intelligence is able to find patterns in speech or writing, and following predetermined parameters, establish if they present small changes, indicators of neurodegenerative diseases in their early stages, allowing patients to be diagnosed early, anticipating treatments over a wide range time until the onset of the first symptoms.

Methods. This paper is a review about the theme "New Technologies in the Neurodegenerative Diseases Prevention". To do this study, we researched articles in Schoolar Google, published between 2015 and 2020, restricting analysis to articles written in languages: English and Portuguese. Over the course of the investigation, more than 100 articles were found, during the period, 30 articles were selected for pre-analysis, among them divided into thematic groups. There is a scarcity of data that investigate these factors in view of this. The present study is expressive for the development of solutions that assist in the neurodegenerative diseases.

Results and Discussion.

Parkinson's Disease Early Diagnosis Development

The flexible platinum electrodes, used by UFSCar researchers, are capable of showing signs that the patient has a tendency to develop Parkinson's. The test is done by inserting a sample of dopamine, collected from the patient, into the electrode, which will check, through electrochemical analysis, whether there are divergences from the standard values of certain biomarkers present in the body. The analysis procedure is feasible due to the role of the DJ1 protein in blocking nerve synapses, showing dysfunctions by causing tremors in the patient's body. (G1 SÃO CARLOS E ARARAQUARA, 2020). (Our translation)

Although clinical tests with patients with the disease are still required and should be expanded to hospitals and pharmaceutical industries, the experiment proved to be quite promising and effective, given the laboratory tests performed on synthetic samples and the good results presented during the period of a year.

It is an innovative device, fully portable and applicable in any medical clinic, hospital or laboratory, being able to provide a diagnosis within an average of five hours and can be practically discarded, given the material of its composition, designed to be sustainable.

Alzheimer's Early Diagnosis Development

The research was divided into three parts, the first being carried out by a researcher at the University of Lund, located in Sweden. In this first study, carried out with people, plasma p-tau217, present in the blood and classified as a highly accurate biomarker in the diagnosis of Alzheimer's, was used as the basis for the experiment. The study proved that the test was as effective as the tests currently used to detect the disease. (ALVES, 2020). (Our translation)

Numerous cases of patients who were diagnosed with Alzheimer's disease were studied, comparing the results found from experiments with biomarkers present in the blood, with the results of imaging exams.

However, it has been found that by analyzing only p-tau217 plasma it is possible to diagnose Alzheimer's with an accuracy of up to 98%, ruling out any chances of attributing the symptoms to other neurodegenerative diseases. (ALVES, 2020). (Our translation)

Alzheimer's tends to cause p-tau217 levels to grow exponentially, and in patients who have a characteristic gene for the disease, plasma begins this expansion process many years before symptoms begin to appear.

In the second research study, carried out by researchers at the University of Washington, in the United States, the role that beta-amyloid proteins and plasma p-tau217 play in the body was investigated. The p-tau217 was fully analyzed by the researchers, who were able to verify that it

is strongly associated with the concentration of amyloid plaques found in the region of the brain, which is affected by the disease. (ALVES, 2020).

In the third study, carried out by specialists from the University of California, in the United States, analysis were carried out with the plasma p-tau181, which found its presence in amounts up to three times greater in people diagnosed with Alzheimer's, when compared to the levels of the plasma in healthy people, or diagnosed with other types of neurodegenerative diseases, making this characteristic of the disease and helping in its early diagnosis. (ALVES, 2020).

Given the three studies, carried out by researchers from several universities, it was proven that the amounts of plasma p-tau217 and p-tau181 present in the blood can be used as biomarkers to aid in the diagnosis of Alzheimer's disease, or other neurodegenerative diseases (by the exclusion factor of the possibility of being Alzheimer).

Development of Artificial Intelligence in the early diagnosis of Neurodegenerative Diseases

Most neurodegenerative diseases often end up being diagnosed only at more advanced stages, due to the complexity of identifying exactly which disease is in question, given its similarities, in order to initiate the appropriate treatment. The insertion of AI in the field of diagnostic imaging has the ability to identify neurodegenerative diseases in patients in advance, and it can even calculate with some precision how much the disease will develop over the years and how much it will affect the patient (SUMMIT SAÚDE, 2020). However, these data can be avoided, given the previous diagnosis made by the AI, allowing the patient to start the treatment in advance.

Based on machine learning, it is possible that an AI is able to identify more and more aspects of neurodegenerative diseases, whether by imaging exams, capturing movements, or analyzing how the patient pronounces words. The potential of an AI in this area has the chance to go beyond the analysis capacity of any specialist, being a tool that could provide extremely fast and accurate diagnoses, so that the responsible professional could also work more efficiently in relation to what treatment to provide for their patients.

Final Thoughts: Due to the high number of people suffering from neurodegenerative diseases today and the fact that this number will only tend to grow in the coming years, we are slowly heading towards a health system failure, which highlights an urgent need for practical, effective diagnostic tools and that anticipate the onset of this type of disease. (BRUM, 2018). The most viable solution to solve this problem is to invest in new technologies that are emerging, such as those presented in this article, for the prevention and early treatment of such neurological diseases, like Parkinson's Disease and Alzheimer's, which are the most recurrent in elderly population worldwide.

From the new exam models shown, there is the possibility of early detection of neurodegenerative diseases, to intervene with effective treatments and delay their progress, preventing significant damage from being caused to the patient's brain, favoring a better quality of life for the patients themselves and their families, consequently also preventing a collapse in our health care system.

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