Chapter 5

Current Biosensor Designs and Applications For Early Detection of Neurodegenerative Diseases

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Abstract

The most common neurodegenerative diseases worldwide are Alzheimer's and Parkinson's. These diseases occur when the brain and peripheral nervous system gradually lose their function or result in the death of nerve cells. Thus, a healthy life depends on the early detection of neurodegenerative illnesses. Because of the high expense, limited sensitivity, and drawbacks of conventional diagnostic techniques, currently available biosensor technologies enable the development of alternative techniques for the early identification of neurodegenerative illnesses. Biosensors make it possible to quickly, sensitively, and usually non-invasively identify biomarkers of certain neurodegenerative disorders by using bioreceptors and transducers (optical, piezoelectric and electrochemical techniques). Together with these biomarkers, exosomal microRNA and Tau oligomer biomarkers also make effective detection possible. A thorough analysis of research employing biosensor technology for the early detection of neurodegenerative illnesses is provided in this section. These include discussion of several biosensor kinds, their operation, clinical uses with various immobilization techniques, and upcoming advancements.

1. Introduction

Neurodegenerative diseases include Alzheimer's disease (AD), Parkinson's disease (PD), prion disease, motor neuron disease (MND), Huntington's disease (HD), spinocerebellar ataxia (SCA), and spinal muscular atrophy (SMA) (1). Affecting 55 million people worldwide, the most common are Alzheimer's and Parkinson's disease. Statistics show that these diseases increase with age. Among individuals aged 65-85, the prevalence of these diseases doubles every five years (2,3). Genetic factors

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should also be considered. Types of neurodegenerative diseases and their causes are illustrated in Figure 1 and 2.

Symptoms observed in individuals with neurodegenerative diseases include

- Physical and behavioral decline
- Decreased mental function
- Behavioral problems

Biosensors are systems that find specific substances using a biological part and a sensor, giving quick and accurate results without needing extra chemicals (4). Electrochemical biosensors offer various applications for easy-to-use, low-cost, and portable devices for medical diagnosis (5). Piezoelectric biosensors are systems that utilize biological components as coating materials and incorporate piezoelectric crystals (6). Optical biosensors are sensor systems that transform light by refraction, absorption, and reflection (7). Biosensor designs developed with current technology have many applications. Biosensors are used in many areas, including the military, food, the chemical industry, healthcare, and environmental analysis (8).

This chapter examines new biosensor technologies for early detection of neurodegenerative diseases, focusing on biomedical engineering, operating principles, applications, and future prospects.

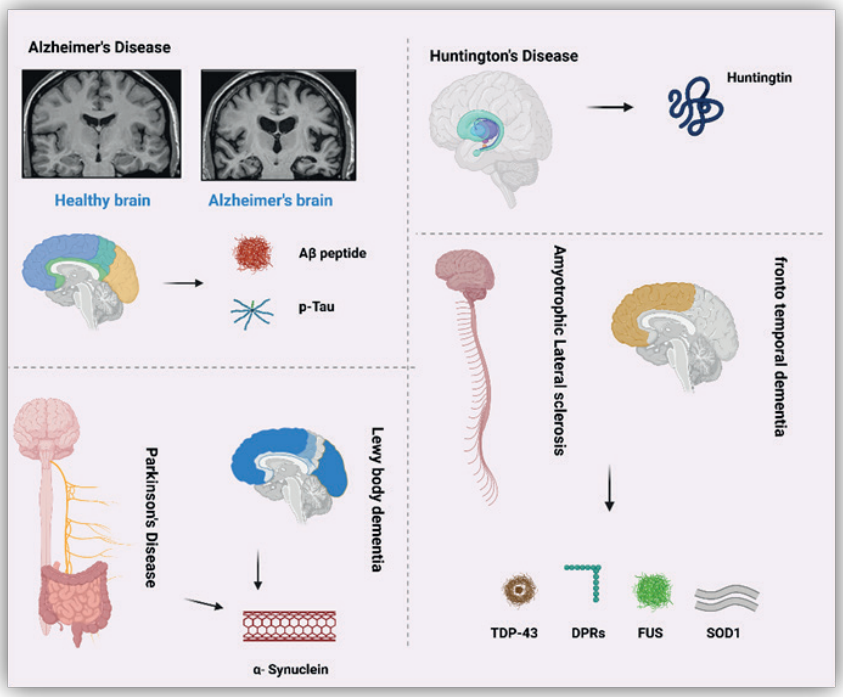

Figure 1: Neurodegenerative diseases and their effects (Created in https://BioRender.com)

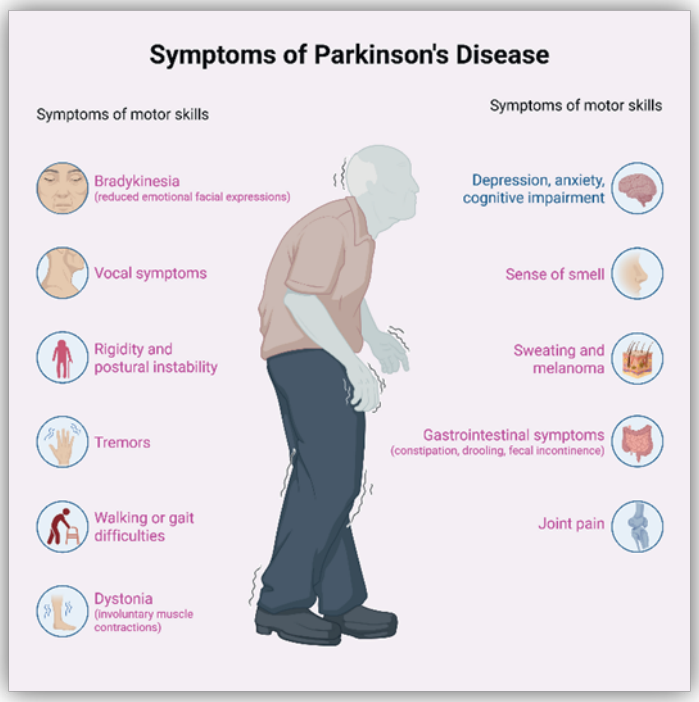

Figure 2: Symptoms of PD, a neurodegenerative disease (Created in https://BioRender.com)

2. Biosensor systems for early diagnosis of neurodegenerative diseases

Biosensors are recognition systems designed to identify bioreceptors and analytes. When transducers interact with receptors, a measurable signal is generated. These transducers transmit signals by assessing the conductivity of surfaces after receiving electrical, optical, or electrochemical inputs. The efficiency of signal transfer depends on the surface conductivity. A large surface area and the capacity to detect conductivity are the primary reasons why carbon materials are preferred in biosensor studies for this purpose. Additionally, graphene-based nanomaterials may be advantageous for signal conversion and sensor surface binding. However, enzymes can only achieve surface binding through physical adsorption (9).

Nanotubes, AuNPs, quantum dots, and GO are among the numerous nanomaterials that are included in the category of biosensors, as indicated by numerous studies. Researchers extensively employ biosensors in the

early diagnosis of neurodegenerative diseases and in the detection of AD in cerebrospinal fluid (CSF) (10). Recent advancements in nanomaterials, biorecognition components, and microfabrication techniques have advanced the area, paving the way for the development of biosensors that are more useful and efficient in clinical settings.

Haşvin et al. (11) investigated protein misfolding to investigate the causes of AD and PD. They designed optical and electrochemical biosensors using carbon nanotubes and gold nanoparticles. They used them to detect Aβ40/Aβ42, tau, ApoE, and miRNA markers in CSF and blood. In different study, Karaboğa et al. (12) designed a disposable electrochemical biosensor for the early diagnosis of Parkinson's-type dementia using alpha-synuclein protein. The study used an ITO-PET electrode modified with AuNPs and glutamic acid as the working electrode. Furthermore, the study was expected to aid in disease diagnosis by sensitively detecting the protein in CSF. The biosensor's linear detection range was 4-200 pg/mL, and the limit of detection was 0.135 pg/mL.

Jose et al. (13) developed an electrochemical biosensor using the misfolding method of tau protein. This study aimed to determine how tau protein in solution binds to immobilized tau protein, using surface characterization data to assess electrostatic changes. While the charge transfer resistance (Rct) of tau protein was determined to be 2.9 ± 0.6 kΩ, it was observed that the resistance (Rct) formed after Tau-Tau binding decreased to 0.3 ± 0.1 kΩ. A linear relationship was observed between (Rct) and the solution tau concentration (0.2–1.0 μM).

Aminabad et al. (14) designed an electrochemical biosensor system for the determination of alpha-synuclein protein. In this study, they created an AuNP-supported dimethylglyoxime layer on a GCE surface to facilitate antigen-antibody interaction. The linear detection range of the designed immunosensor was 4-128 ng/mL, and the limit of detection value was determined to be 4 ng/mL.

In different study Karaboğa et al. (15) developed an immunosensor for the selective and practical analysis of α-synuclein protein. This study's working electrode represents an innovative approach to modern technology. The working electrode used was gold-coated QTF electrodes. QTFs were obtained by conjugation with 4-ATP (aminothiophenol). The linear detection range was 1-500 ng/mL, and the limit of detection was 0.098 ng/mL. Since the QTF uses a mass-sensitive biosensor system, it was able to recover 92%-104% of the samples taken from CSF for the designed sensor. Tao et al. (16) used a GCE to immobilize anti-α-synuclein antibodies by

creating a composite of polyglycosamine, AuNPs, carbon nanotubes, and reduced GO. In this work, a square-wave voltammetry method was used to create an immunosensor. The sensor was found to have a linear range of 0.05-500 fM and a limit of detection of 0.03 fM. Human plasma samples were used for testing the developed sensor.

Chandra et al. (17) designed short microRNA (mRNA) sensors associated with Parkinson's disease. Using miR133b as a biomarker, the ssDNA sequence was tagged, and the process of oxidation and reduction was observed with tris phosphine hydrochloride. The optimum sensor was determined to have a linear range of 10 fM-520 pM and LOD of 168 aM. In different study Raquel et al. (18) designed an electrochemical microRNA sensor using carbon SPE electrodes with two gold nanostructures and an anti-miR-34a OP. The linear range of this biosensor was determined to be 100 pM-1μM, and the LOD value was determined to be 93 aM. In another study, Wang et al. (19) developed an electrochemical biosensor that supports antigen-antibody formation on gold microstrip electrodes coated with protein G. The EIS technique was used for analysis in the study. The study demonstrates that the designed biosensor can detect tau protein levels as low as 0.03 pM.

Table 1. The biosensor systems for early diagnosis of neurodegenerative disease

Targets	Measurement method	Modification method	Linear range	Reference
Aβ40/Aβ42, tau, ApoE, and miRNA	Electrochemical & Optical	Modification with carbon nanotubes and gold nanoparticles.	-	(11)
α- synuclein	Electrochemical	Modification with AuNP and glutamic acid in ITO-PET	4-2000 pg mL^{-1}	(12)
Tau	Electrochemical	Tau-Tau	0.2–1.0 μM	(13)
α- synuclein	Electrochemical	AuNP-supported dimethylglyoxime layer on a GCE surface	4-128 ng mL^{-1}	(14)
α- synuclein	Electrochemical	Modification with 4ATP in QTF	1-500 ng mL^{-1}	(15)
α-synuclein	Electrochemical	Modification with nanocomposite polyglycosamine, AuNPs, carbon nanotubes, and reduced graphene oxides	0.05 -500 fM	(16)
miR133b	Electrochemical	Ss DNA	10fM-520 pM	(17)
miR-34a	Electrochemical	Carbon SPE	100 pM-1μM	(18)
Tau	Electrochemical	The gold microband electrodes	0.03 pM	(19)

3. Conclusions

The challenge of researching the central nervous system leads to neurodegenerative illnesses. The quality of life for these individuals will be greatly enhanced by facilitating this difficulty and increasing the success of early diagnosis and treatment. Biomarkers used in the diagnosis of targeted neurodegenerative diseases through the integration of biosensors, bioreceptors, and transducers can be detected rapidly, sensitively, and cost-effectively. Electrochemical, optical, and piezoelectric biosensors are proving highly successful in the diagnosis of new-generation biomarkers and their use in various blood, such body fluids, brain, spinal fluid, and tears. In addition, while the designed biosensors have strong potential for early diagnosis, clinical validation is ongoing due to the unexplored areas of the brain and nervous system.

In conclusion, biosensor technologies will not only expand the possibilities of early diagnosis in neurodegenerative diseases through routine clinical application but will also contribute to the development of patient- and disease-specific treatment options.

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