Development of Wearable Biosensors for Continuous Monitoring of Neurological Biomarkers

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Abstract

The field of wearable biosensors has witnessed remarkable advancements in recent years, revolutionizing healthcare by enabling continuous monitoring of various physiological parameters. Among the many applications, the monitoring of neurological biomarkers stands out as a critical area of research and development. This review article provides a comprehensive overview of the progress made in the development of wearable biosensors for continuous monitoring of neurological biomarkers. We discuss the significance of monitoring neurological biomarkers, explore the key challenges faced in this domain, and highlight the emerging technologies and strategies that have paved the way for innovative solutions. Moreover, we delve into the potential clinical applications and future prospects of wearable biosensors in the field of neurology.

Significance | Continuous monitoring of neurological biomarkers via wearable biosensors offers early disease detection, personalized treatment, and enhanced patient outcomes, revolutionizing neurology.

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Introduction

The human nervous system plays a pivotal role in maintaining overall health. Neurological biomarkers are molecules that can be measured in the body to provide information about the health of the nervous system (Chaves, A.R. *et al.* 2021). Monitoring these biomarkers offers numerous advantages, including the early detection of diseases before symptom onset, tracking disease progression, assessing treatment efficacy, identifying individuals at risk of neurological disorders, and enhancing our understanding of neurological disease pathophysiology (Qiu, Shi, et al., 2023).

Continuous monitoring of neurological biomarkers is especially crucial given the challenges associated with diagnosing and treating neurological diseases (Tripathi, Akhilesh Kumar, et al., 2023). These disorders are a leading global cause of disability and mortality, and their prevalence is projected to rise with an aging population (Wang, Haidong, et al., 2016). Conventional methods for monitoring neurological biomarkers, such as blood tests and imaging, are invasive, intermittent, and cost-prohibitive, rendering them unsuitable for continuous surveillance. To address this need, wearable biosensors have emerged as non-invasive, continuous monitoring devices that can be worn by patients in their everyday environments (Vijayan, Vini, et al., 2021).

The development of wearable biosensors for continuous neurological biomarker monitoring is gaining momentum due to several factors. These include the increasing incidence of neurological diseases like Alzheimer's disease, Parkinson's disease,

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and multiple sclerosis, the urgent need for timely diagnosis and treatment, and the desire to enhance the quality of life for individuals living with these conditions (Iqbal, S. M., et al., 2021). Although wearable biosensors for neurological biomarker monitoring are still in the early stages of development, substantial progress has been made in recent years (Topol, Eric J., 2019). Several companies are actively working on these devices, some of which have already entered clinical trials. These advancements hold great promise for revolutionizing the way we diagnose, manage, and treat neurological diseases, ultimately improving patient outcomes and enhancing our understanding of these complex conditions (Woelfle, Tim, et al., 2023).

This review article will discuss the development of wearable biosensors for continuous monitoring of neurological biomarkers. We will provide an overview of the different types of wearable biosensors that are being developed, discuss the recent advances in this field, and highlight the challenges and future directions.

2. Neurological Biomarkers: A comprehensive exploration

Neurological biomarkers are molecules or physiological parameters that can provide information about the health and functioning of the nervous system. These biomarkers may include neurotransmitters, proteins, electrical signals (EEG), and various metabolic indicators. They have emerged as crucial tools in the field of neuroscience and clinical medicine, offering insights into the intricacies of the nervous system's structure and function.

2.1. Significance of Neurological Biomarkers:

Neurological biomarkers are molecules, compounds, or physiological indicators that can be detected and measured in biological samples, such as blood, cerebrospinal fluid, or tissues. They provide valuable information about the health and functioning of the nervous system. These biomarkers serve as critical tools for clinicians, researchers, and healthcare professionals for several reasons:

2.1.1. Early Disease Detection: Neurological biomarkers can detect abnormalities in the nervous system before clinical symptoms manifest (Meschia, James F., et al., 2023; Avni and Muhit, 2022). This early detection is especially crucial for neurodegenerative diseases like Alzheimer's and Parkinson's, where intervention at an early stage can significantly impact disease progression. Table 1 provides an overview of various neurological biomarkers, their associated diseases, and the diagnostic procedures or methods used for early disease detection. It highlights the importance of these biomarkers in diagnosing neurological conditions and the diverse diagnostic techniques employed in clinical practice and research to enable early intervention and improved patient outcomes.

2.1.2. Disease Monitoring with Neurological Biomarkers: Biomarkers help physicians keep a close eye on how a disease is getting worse or better, which is crucial for tailoring treatments to individual patients. In neurological conditions, like those affecting the brain and nerves, these biomarkers are helpful tools that provide important information about how the disease is changing, how well treatments are working, and how to best take care of patients. By monitoring neurological biomarkers, physicians can detect disease early (Winblad, Bengt, et al., 2004), before symptoms develop (Suárez-Calvet, Marc, et al., 2016), track disease progression over time (Gold, Larry, et al., 2010), assess the effectiveness of treatments (Bartolomucci, Alessandro, et al., 2010), identify individuals at risk of developing neurological diseases (Winblad, Bengt, et al., 2004) and provide more personalized and effective care to patients (Albert, Marilyn, et al., 2011).

2.1.3. Research Advancements: Neurological biomarkers are essential tools for advancing research on neurological disorders (Tripathi, Akhilesh Kumar, et al., 2023). They provide insights into the underlying mechanisms and disease processes of a wide range of neurological conditions (Winblad, Bengt, et al., 2004). Biomarkers can reveal unique molecular and physiological signatures within the nervous system, shedding light on the complexities of disease onset, progression, and pathophysiology (De Mello Rieder, Marcelo, et al., 2019). This knowledge can be leveraged to identify novel targets for therapeutic intervention. With the aid of neurological biomarkers, researchers are better equipped to develop innovative treatments and interventions that can improve the lives of individuals affected by neurological disorders (Kim, Bokkyu, and Carolee J. Winstein, 2016).

3. Neurological biomarker relevance in neurological Conditions:

Neurological biomarkers find applications in a wide array of neurological conditions which are medically important as discussed below:

3.1. Neurodegenerative Diseases: Neurodegenerative diseases are a group of diseases that cause progressive damage to the nervous system, including the brain, spinal cord, and nerves. These diseases can lead to a variety of symptoms, such as cognitive decline, movement disorders, and sensory loss. As given in table 2, biomarkers help diagnose Alzheimer's, Parkinson's, and other neurodegenerative diseases, as well as monitor disease progression and treatment response (Tripathi, Akhilesh Kumar, et al., 2023).

3.2. Epilepsy: Epilepsy is a chronic neurological disorder characterized by recurrent seizures. A seizure is a sudden, abnormal electrical discharge in the brain that can cause a variety of symptoms, such as loss of consciousness, muscle contractions, and sensory disturbances. EEG biomarkers aid in diagnosing epilepsy, determining seizure types, and assessing treatment effectiveness (Moshé, Solomon L., et al,. 2015).

3.3. Stroke: Biomarkers in blood and cerebrospinal fluid assist in diagnosing strokes and predicting outcomes. In addition to diagnosing strokes, blood and cerebrospinal fluid biomarkers can also be used to predict outcomes. For example, higher levels of CRP and IL-6 in the blood are associated with a higher risk of death and disability after a stroke. Higher levels of neutrophils in the cerebrospinal fluid are also associated with a higher risk of death and disability after a stroke (Kim, Bokkyu, and Carolee J. Winstein., 2016).

3.4. Biomarkers for Traumatic Brain Injury: Biomarkers for traumatic brain injury (TBI) are substances that can be measured in the blood or cerebrospinal fluid (CSF) to indicate the presence or severity of a TBI. Biomarkers can be used to diagnose TBI, assess the severity of the injury, monitor the recovery process, and predict outcomes. Table 2 provides an overview of biomarkers for traumatic brain injury (TBI).

4. Applications of Biomarkers in Continuous Neurological Monitoring.

Continuous neurological monitoring (CNM) is a process of tracking changes in brain activity and other neurological functions over time. CNM can be used to monitor patients with a variety of neurological conditions, such as stroke, epilepsy, and traumatic brain injury. Biomarkers can be used to detect changes in brain activity, assess the severity of neurological damage, and monitor the response to treatment.

4. 1. Role of biomarkers in CNM:

4.1.1. Detect changes in brain activity: Biomarkers can be used to detect changes in brain activity that may be associated with seizures, stroke, or other neurological conditions. This can help clinicians to identify and treat problems early, before they cause permanent damage. For instance, biomarkers such as S100B and NSE can be used to detect stroke early, assess the severity of the stroke, and monitor the response to treatment. According to a study conducted by Shinozaki, Koichiro, et al., serum levels of protein neuron-specific enolase (NSE) and S-100B could be considered promising candidates for neurological prognostic predictors in patients with ROSC after CPR, and many investigations on the clinical usefulness of these biochemical markers in predicting neurological outcomes after CPR have been published (Shinozaki, Koichiro, et al., 2009). The study by Thelin, Eric P., et al., suggests that S100B has successfully been implemented in the clinic regionally (1) to screen mild TBI patients evaluating the need to perform a head computerized tomography, (2) to predict outcome in moderate-to-severe TBI patients, (3) to detect secondary injury development in brain-injured patients and (4) to evaluate treatment efficacy (Thelin, Eric P., et al., 2016).

4.1.2. Assess the severity of neurological damage: Biomarker levels can be used to assess the severity of neurological damage. This information can be used to guide treatment decisions and predict patient outcomes. According to Lleó, A. (2021), biomarkers have been progressively incorporated into clinical routine and clinical trials in the field of neurology (Lleó, Alberto, 2021). Another study by Papa, L., & Ramia, M. M. (2017), suggests that biomarkers can be used to detect and predict the severity of traumatic brain injury (TBI) in athletes after sports-related concussion. The study focuses on five of the most commonly studied markers for mild TBI: glial fibrillary acidic protein (GFAP), neurofilament light chain protein (NF-L), ubiquitin C-terminal hydrolase-L1 (UCH-L1), tau, and S100B (Papa, Linda, et al., 2015).

4.1.3. Monitor the response to treatment: Biomarker levels can be used to monitor the response to treatment. They can be used to track the effectiveness of a treatment, identify patients who are more likely to respond to a particular therapy, and monitor the progression of a disease. This information can be used to adjust treatment as needed and ensure that patients are receiving the most effective care. Nisar, Sabah, et al. (2020), discussed the use of non-invasive imaging biomarkers for monitoring the immunotherapeutic response to cancer. The authors suggest that quantitative imaging technologies that interrogate T cell responses, metabolic activities, and immune microenvironment could offer a powerful tool to monitor the cancer response to immunotherapy (Nisar, Sabah, et al., 2020). Another study describes various circulating biomarkers that can be used for therapeutic monitoring of anti-cancer agents. The authors highlight non-specific markers of disease burden, tumor markers (e.g. CA 125, CEA, PSA, etc.), circulating tumor cells, nucleic acids, exosomes, and metabolomic arrays (Van Rensburg, et al., 2022).

5. Emerging Developments and Breakthroughs in Neurology Biomarker Research.

Wearable biosensors are devices that can be worn on the body to continuously monitor biomarkers. They have the potential to revolutionize the diagnosis, management, and treatment of neurological diseases (Janghorban, Mohammad, et al., 2022). The development of biosensors for neurological biomarkers faces several challenges, including sensor accuracy, data reliability, and user acceptance. Ensuring that these sensors provide accurate and clinically relevant data is essential for their widespread adoption. Moreover, ensuring data privacy and security is crucial, as continuous monitoring raises concerns about data protection and unauthorized access.

5.1. *Challenges in Neurological Biomarker Biosensor Technology.*

One of the biggest challenges is ensuring that biosensors provide accurate and clinically relevant data. This is difficult because neurological biomarkers are often present in very low concentrations in bodily fluids, and biosensors need to be able to distinguish between different biomarkers and to avoid interference from other substances in the body. Some researchers are developing wearable biosensors that can measure multiple biomarkers simultaneously (Gao, Wei, et al., 2016). This can help to improve the accuracy of diagnoses and to reduce the risk of interference from other substances in the body. Additionally, researchers are developing new ways to filter out noise and interference from the data collected by biosensors (Nam, Dahyun, et al., 2021).

Another challenge is ensuring that biosensors collect data reliably. This means that the sensors need to be able to function accurately and consistently over time, even in a variety of environmental conditions. Now in order to improve data reliability, some researchers are developing wearable biosensors that can self-calibrate. This means that they can automatically adjust their settings to ensure that they are providing accurate data (Kivirand, Kairi, et al., 2013). Additionally, these researchers have developed new ways to power wearable biosensors for extended periods of time without the need for batteries (Song, Yu, et al., 2021).

For biosensors to be widely adopted, they need to be easy to use and comfortable for patients to wear. Additionally, patients need to be confident in the accuracy and reliability of the data collected by the sensors. So, in order to improve user acceptance, some researchers are developing wearable biosensors that are integrated into wearable devices, such as smartwatches and fitness trackers. This would make it easier for patients to wear the sensors and to track their data over time (Smith, Aaron Asael, et al., 2023).

Continuous monitoring of biomarkers raises concerns about data protection and unauthorized access. It is important to ensure that data is collected, stored, and transmitted in a secure manner. For protection of data privacy and security, some researchers are developing encryption algorithms to protect the data from unauthorized access. Additionally, researchers are developing new ways to allow patients to have control over their data and to opt out of data collection at any time (Jiang, Dawei, and Guozhen Shi, 2021).

The table (Table 3) above provides a summary of cutting-edge wearable biosensor technologies that are being developed for neurology. These technologies have the potential to revolutionize the way that neurological diseases are diagnosed and managed.

5.2. Emerging trends and innovations in wearable biosensors for continuous monitoring of neurological biomarkers

The continuous advancement in wearable biosensors for monitoring neurological biomarkers has introduced several significant trends and innovations, shaping the landscape of modern healthcare. These pivotal developments reflect the cutting-edge progress within the field:

5.2.1. Advanced Sensor Technologies:

Advanced sensor technologies leverage nanomaterials and microfluidics to achieve unprecedented sensitivity and specificity in detecting neurological biomarkers (Wang, Jiayu, and Jianfei Dong, 2020). Nanomaterials, due to their incredibly small scale, exhibit exceptional properties that revolutionize sensor capabilities. These materials offer an extensive surface area and unique physical and chemical properties, allowing for enhanced interaction with biological elements. By leveraging nanomaterials, sensors can capture and identify even minute quantities of neurological biomarkers, amplifying the sensitivity of detection to previously unparalleled levels (Adam, Tijjani, et al., 2023).

Complementing this innovation, microfluidics plays a crucial role in sensor functionality. Microfluidics involves the precise control and manipulation of tiny amounts of fluids within minuscule channels or chambers. This technology facilitates the controlled movement, mixing, and analysis of biomarker samples, enabling a highly efficient and accurate detection process. The ability to handle these samples at such a minute scale ensures that even trace amounts of biomarkers can be captured and analyzed with exceptional precision (Stangler, Luke A., et al., 2021).

Together, the amalgamation of nanomaterials and microfluidics within sensor technologies enables an unprecedented level of sensitivity and specificity in the detection of neurological biomarkers. This marriage of technologies significantly enhances the ability to identify and analyze these biomarkers with remarkable accuracy, offering a promising pathway for earlier and more precise diagnosis of neurological conditions. Ultimately, this innovation holds significant potential for advancing healthcare by providing more effective and timely interventions for improved patient outcomes.

5.2.2. AI and Machine Learning Integration:

The integration of AI (Artificial Intelligence) and Machine Learning technologies stands as a game-changer in the analysis of real-time data streams captured by wearable biosensors, particularly in the realm of neurological abnormalities (Vijayan, Vini, et al., 2021). These cutting-edge technologies excel in swiftly processing vast amounts of data, identifying patterns, and learning from the information collected. This capability empowers a proactive approach to healthcare by enabling early detection and even predictive abilities for neurological irregularities (Mishra, Saurav, 2022).

AI algorithms, functioning in real-time, continuously process incoming data from wearable biosensors. They swiftly recognize deviations or patterns that might indicate potential neurological abnormalities. By learning from the data patterns, these algorithms become adept at flagging potential issues well before noticeable symptoms might occur. This early detection is invaluable, as it enables timely intervention and proactive measures, potentially preventing or mitigating the progression of neurological disorders (Krauhausen, Imke, et al.,2023).

Moreover, the predictive capacity of AI and Machine Learning is instrumental. These technologies can analyze historical data, learn from patterns, and forecast potential neurological issues based on established trends. By recognizing changes or deviations in these patterns, they can predict the likelihood of certain neurological abnormalities, allowing for early alerts and proactive medical interventions.

5.2.3. Miniaturization and Portability:

Advancements in microelectronics and materials science have played a pivotal role in shrinking the size of wearable biosensors, leading to discreet and portable devices that significantly enhance user comfort. The progress in these fields has allowed for the development of smaller, lighter, and more efficient sensor components (Lázaro, Antonio, et al., 2023).

Microelectronics advancements have led to the creation of incredibly tiny yet powerful electronic components. These miniature components, such as processors, memory, and sensors, offer high functionality while occupying minimal space. Additionally, they require less power to operate, contributing to the creation of smaller yet long-lasting wearable devices. Moreover, breakthroughs in materials science have introduced new lightweight and flexible materials. These materials are not only durable but also comfortable when in contact with the skin. Their flexibility allows the sensors to conform to the body's contours, making them less obtrusive and more comfortable for extended wear. Furthermore, these materials often exhibit biocompatibility, meaning they are safe for prolonged contact with the skin and reduce the risk of adverse reactions (Lin, Wenzhou, et al., 2023).

The miniaturization of these wearable biosensors translates into discreet, less cumbersome, and more user-friendly devices. Their smaller size and lightweight nature make them nearly imperceptible, promoting user comfort and wearability for extended periods. This transformation in size and comfort encourages user compliance with continuous monitoring, as the devices seamlessly integrate into everyday life without causing discomfort or hindrance.

Figure 1 demonstrates thoughtfully examining how biosensors process signals and the speed at which reactions move within them, it becomes feasible to create strategies at both the structure and device levels. These strategies can harness the advantages of making biosensors smaller, resulting in biosensors that can both detect very small amounts of substances and provide quick responses (Soleymani, Leyla, and Feng Li, 2023).

***5.2.4. Biocompatible Materials*:**

Continual exploration and development of biocompatible materials have led to substantial advancements in enhancing the safety and comfort of wearable biosensors. Biocompatible materials are specifically designed to interact harmoniously with the human body, ensuring safety, comfort, and reduced risk of adverse reactions when in contact with the skin. The properties of these biocompatible materials contribute to the comfort of wearable biosensors. They are often soft, flexible, and lightweight, making them pleasant to wear. Their flexibility allows the sensors to mold comfortably to the body's contours, ensuring a snug fit without causing discomfort or restricting movement. Moreover, some of these materials possess breathability, allowing air circulation and reducing moisture buildup, which further adds to user comfort during extended use (Mathew, Minu, et al., 2020).

***5.2.5. Real-time Connectivity and Data Sharing*:**

The emphasis on real-time connectivity and data sharing is pivotal. Wearable biosensors are now designed to synchronize with various digital platforms, providing patients and healthcare providers with immediate access to vital data (Abubeker, K. M., and S. Baskar, 2022). This connectivity fosters prompt decision-making and patient empowerment. The emphasis on real-time connectivity and data sharing holds significant importance in the realm of wearable biosensors. Real-time connectivity enables wearable biosensors to sync and communicate instantly with other devices, such as smartphones, tablets, or computers. This connectivity allows for the swift transmission of data collected by the sensors. When data is shared in real-time, it provides immediate access to vital information for both the users of the device and healthcare providers (Smith, Aaron Asael, et al., 2023). This immediate access to real-time data is particularly vital in healthcare scenarios. For instance, in the case of continuous health monitoring, such as tracking neurological biomarkers or vital signs, the ability to access and interpret this data instantly is invaluable. It allows for timely decision-making, early detection of abnormalities, and immediate response in case of emergencies.

6. Future Directions in Neurobiomarker Monitoring.

The continuous evolution of neurobiomarker monitoring through wearable biosensors opens up compelling avenues for future exploration and development. Examining the potential future directions in this field reveals promising advancements and opportunities:

6.1. Multimodal Sensor Integration:

The integration of multimodal sensors in neurobiomarker monitoring represents a significant leap in the breadth and depth of data collection for neurological health. This approach may involve combining various sensor types, such as EEG (Electroencephalography), ECG (Electrocardiography), and biochemical sensors, to capture a more comprehensive spectrum of neurological information. By merging these diverse sensor technologies, it becomes possible to gather multifaceted data, including brain activity, cardiac functions, and specific biomolecular indicators, offering a more holistic view of neurological health. Multimodal sensor integration not only enhances the accuracy and precision of neurobiomarker monitoring but also provides a more thorough understanding of neurological conditions, potentially leading to more precise diagnoses and personalized treatment strategies (Kuhn, Christopher B., et al., 2022).

6.2. Real-time Data Analytics and Predictive Modeling:

Advancements in real-time data analytics and predictive modeling using machine learning algorithms are expected to mature further

(Singh, Umesh Pratap, 2022). Real-time data analytics and predictive modeling play a vital role in the early identification and anticipation of neurological abnormalities. By continuously analyzing data in real-time obtained from various sources such as wearable biosensors or medical records, advanced algorithms can swiftly process and detect irregular patterns or deviations. This immediate data analysis enables the identification of potential neurological anomalies at their early stages, even before noticeable symptoms appear. Furthermore, through predictive modeling, these algorithms can recognize trends and patterns in neurological data, aiding in forecasting potential abnormalities. Detecting these subtle changes in data patterns allows for proactive medical interventions and timely treatments, potentially averting the progression of neurological disorders and enhancing patient care outcomes (Kim, Heena, et al. 2023).

By following participants longitudinally, researchers can gather comprehensive and detailed data on the performance of these biosensors. This data helps in understanding the device's consistency over time, its response to different physiological changes, and its usability in diverse scenarios. Additionally, these studies aid in evaluating the practicality and acceptance of the technology among both patients and healthcare providers.

6.4. Development of User-friendly Interfaces and Applications:

Emphasis on user-friendly interfaces and applications will be a key focus. Efforts to enhance the usability and accessibility of these wearable devices, ensuring seamless integration with smartphones and user-friendly interfaces, will be critical in promoting patient engagement and adherence to continuous monitoring (Tettey, Felix, et al., 2023). Here are a few demonstrations of this concept:

6.4.1. Intuitive Mobile Applications:

Designing mobile apps that accompany wearable biosensors with clear, easy-to-navigate interfaces. These applications display user data in a simple format, providing easy access to real-time information on neurological biomarkers. For example, a health app could feature a dashboard showing daily activity levels or vital signs, easily understandable for users without technical expertise (Chandrashekar, Pooja, 2018).

6.4.2. Customizable Alerts and Notifications:

Creating personalized alerts and notifications on the app that notify users or healthcare providers about any irregularities or significant changes in biomarker levels. For instance, an alert for abnormal heart rate patterns or sudden fluctuations in brain activity could prompt immediate attention or guidance for further actions.

***6.4.3. Seamless Integration with Smart Devices*:**

Developing systems that seamlessly integrate with smart devices, such as smartwatches or smartphones, allowing for easy pairing and data synchronization. This integration ensures that users can effortlessly access their health data and share it with healthcare professionals or family members for monitoring and support (Laaraibi, Abdo-Rahmane Anas, et al., 2023).

The goal of these user-friendly interfaces and applications is to make the process of monitoring neurological biomarkers both accessible and comprehensible for users, thereby improving their engagement and adherence to continuous health tracking.

6.5. Personalized Precision Medicine Integration:

A future trend will revolve around the integration of continuous neurobiomarker monitoring into the concept of personalized precision medicine. By harnessing the wealth of data obtained from continuous monitoring, healthcare can be tailored to the specific needs of individual patients, enabling targeted and personalized treatment strategies (Frey, Lewis J, 2018). The integration of personalized precision medicine in the context of wearable biosensors offers several advantages in healthcare. Here are a few key benefits:

6.5.1. Tailored Treatment Plans:

Personalized precision medicine integrates the data obtained from wearable biosensors to create individualized treatment plans. By considering a person's unique biomarkers and health data, healthcare providers can tailor treatments specific to the individual's needs, leading to more effective and targeted therapies (Ehrenthal, Johannes, 2019).

***6.5.2. Improved Patient Outcomes*:**

Personalized precision medicine, based on data from wearable biosensors, aims to optimize patient care. By providing individualized treatments aligned with a person's health data, it can lead to improved health outcomes, better symptom management, and potentially reduced hospital visits.

6.5.3. Enhanced Patient Empowerment:

Patients become more involved in their healthcare. The access to their own health data and involvement in decision-making processes empowers individuals to actively participate in managing their health. This involvement often leads to better compliance with treatment plans and a deeper understanding of their health status.

6.5.4. Reduced Healthcare Costs:

Tailoring treatments and focusing on preventive measures based on personalized data can potentially reduce healthcare costs. Early interventions and more targeted therapies may lead to less need for invasive treatments, fewer hospitalizations, and overall cost savings for both patients and healthcare systems.

7. Conclusion:

The development of wearable biosensors for continuous monitoring of neurological biomarkers represents a promising frontier in the field of neurology and healthcare. While challenges remain, the progress made thus far offers hope for improved early diagnosis, management, and treatment of neurological conditions. As technology continues to advance, the integration of wearable biosensors into routine clinical practice has the potential to

Table 1. Neurological Biomarkers and Diagnostic Procedures for Early Disease Detection.

Biomarker	Associated Disease	Diagnostic Utility	Diagnostic Procedure/Method	References
Amyloid Beta (Aβ)	Alzheimer's Disease	Early detection and tracking	Cerebrospinal Fluid Analysis, PET Imaging	(Mohanad, Marwa, et al., 2023)
Tau Protein	Alzheimer's Disease	Early detection and monitoring	Blood Tests, Tau-PET Imaging	(Nutma, Erik, et al. 2023, De Leon, Mony J., et al., 2004)
Glutamate	Epilepsy	Seizure prediction and management	EEG, Blood Glutamate Levels	(Sheffrin M, 2016, Curatolo Paolo, et al., 2015)
Oligoclonal Bands	Multiple Sclerosis (MS)	Indicative of immune system activity	Cerebrospinal Fluid Analysis (Isoelectric Focusing)	(Reiber, Hansotto, and James B. Peter, 2001, Modvig, Signe, et al., 2015)
Dopamine Levels	Parkinson's Disease	Reduced levels in basal ganglia	PET Imaging, Dopamine Transporter (DaT) Scans	(Erkkinen, Michael G., et al., 2017, McCutcheon, Robert, et al., 2020)
S100B and GFAP	Traumatic Brain Injury (TBI)	Assessing the severity of brain injury	Blood Tests (Serum S100B, GFAP)	(Zetterberg, Henrik, et al., 2013, Vos, Pieter E., et al., 2010)

Table 2. Applications of Neurological biomarkers in neurological Conditions.

Neurological condition	Biomarkers used	Location	Type of biomarker	Utility	References
TBI	Glial fibrillary acidic protein (GFAP)	Blood, CSF	Protein	Diagnosis, severity assessment, prognosis	(Vos, Pieter E., et al., 2010)
TBI	Ubiquitin C-terminal hydrolase-L1 (UCH-L1)	Blood, CSF	Enzyme	Diagnosis, severity assessment, prognosis	(Bishop, Paul, et al., 2016)
TBI	S100B	Blood, CSF	Protein	Diagnosis, severity assessment, prognosis	(Vos, Pieter E., et al., 2010)
TBI	Neurofilament light chain (NFL)	Blood, CSF	Protein	Diagnosis, severity assessment, prognosis, monitoring	(Modvig, Signe, et al., 2015)
TBI	Tau protein	Blood, CSF	Protein	Diagnosis, severity assessment, prognosis, monitoring	(Buée, Luc, et al., 2000)
Neurodegenerative	Amyloid beta, tau protein, phosphorylated tau protein	Blood, CSF	Protein	Diagnosis, disease monitoring, prognosis	(Buée, Luc, et al., 2000)
Neurodegenerative	Alpha-synuclein, dopamine levels	CSF, brain imaging	Protein, neurotransmitter	Diagnosis, disease monitoring, prognosis	(Goedert, Michel, 2001)
Neurodegenerative	Huntingtin protein	Blood, CSF	Protein	Diagnosis, disease monitoring, prognosis	(Li, Shihua, 2004)
Neurodegenerative	Neurofilament light chain (NFL)	Blood, CSF	Protein	Diagnosis, disease monitoring, prognosis	(Gaetani, Lorenzo, et al., 2019)
Neurodegenerative	Myelin basic protein, oligoclonal bands	Blood, CSF	Protein	Diagnosis, disease monitoring, prognosis	(Boggs, Joan M., 2006, Janssen, John C., et al., 2004)
Stroke	S100B	Blood, CSF	Protein	Diagnosis, severity assessment, prognosis	(Jönsson, Henrik, et al., 2001)
Stroke	neuron-specific enolase (NSE)	Blood, CSF	Protein	Diagnosis, severity assessment, prognosis	(Wunderlich, Michael T., et al., 2006)
Epilepsy	Neurofilament light chain (NFL)	Blood, CSF	Protein	Diagnosis, seizure prediction, prognosis	(Khalil, Michael, et al., 2018)

TBI-Traumatic Brain Injury, CSF- cerebrospinal fluid

Table 3. Emerging Trends in Wearable Biosensor Technologies for Neurology.

Wearable biosensor technology	Biomarkers measured	Target abnormalities	Stage of development	Potential applications	References
Smartwatches and fitness trackers	EEG, MEG, heart rate, blood pressure, blood oxygen levels	Epilepsy, Parkinson's disease, and Alzheimer's disease	Clinical trials	Early detection and diagnosis of neurological diseases, monitoring of disease progression and response to treatment.	(Sharma, Atul, et al., 2021, Aaron Asael Smith, Rui Li & Zion Tsz Ho Tse, 2023)
Headbands and caps	EEG, MEG, NIRS	Epilepsy, stroke, and brain injury	Clinical trials	Early detection and diagnosis of neurological diseases, monitoring of disease progression and response to treatment	(Verma, Deepali, et al., 2022, Ban, Seunghyeb, et al., 2023)
Smart glasses	EEG, eye movement	Parkinson's disease, Alzheimer's disease, and multiple sclerosis	Preclinical development	Early detection and diagnosis of neurological diseases, monitoring of disease progression and response to treatment	(Ha, Minjeong, et al., 2018, Kim, Dawon, and Yosoon Choi, 2021)
Implantable biosensors	Brain activity, blood pressure, other neurological biomarkers	Epilepsy and Parkinson's disease	Preclinical development	Early detection and diagnosis of neurological diseases, monitoring of disease progression and response to treatment, closed-loop brain-computer interfaces	(Ban, Seunghyeb, et al., 2023, Rodrigues, Daniela Sofia Sousa, et al., 2020)

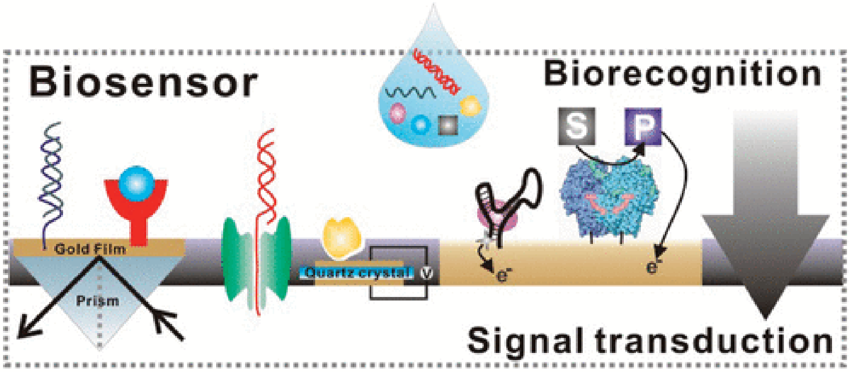

Figure 1. Development of miniaturized biosensors that involves strategies at structural and device levels to achieve high sensitivity and rapid responses. (Adapted with permission from Soleymani, Leyla, and Feng Li, 2023. Copyright (2017) American Chemical Society)

transform the way neurological disorders are monitored and managed.

In this comprehensive review, we have explored the pivotal role of wearable biosensors in continuous monitoring of neurological biomarkers. Understanding the significance of various biomarkers, including proteins, neurotransmitters, and electrical signals, highlights their clinical relevance in diagnosing and managing neurological conditions. Evaluation of wearable biosensor technologies, such as EEG, ECG, and optical sensors, reveals their diverse advantages and limitations, demonstrating their potential applications in neurological monitoring.

We've delved into specific case studies showcasing the efficacy of these biosensors in tracking conditions like epilepsy, Parkinson's disease, and stroke, elucidating their capacity for both quantitative and qualitative data collection. Despite their promising applications, challenges in accuracy, data interpretation, and wearability remain pertinent, alongside ethical and regulatory considerations crucial for ensuring responsible usage.

Moreover, our exploration of emerging trends highlights recent innovations, including AI integration, sensor miniaturization, and improved materials, promising a future of more advanced and efficient biosensors. The clinical applications of these biosensors showcase the potential for personalized, precision healthcare, driving early detection and tailored interventions for improved patient outcomes.

As the field advances, understanding these technologies' potential and limitations is essential for addressing challenges and refining applications. The future direction lies in harnessing these innovations to deliver precise, individualized care, fostering a new era of healthcare that is both proactive and personalized. The continuous development of wearable biosensors for neurological biomarkers stands as a promising frontier in improving healthcare management and patient well-being.

Author contributions

K.H. conceived the study and designed the proposed strategy. K.H. wrote the manuscript. A.K. contributed intellectually to the scientific discussion and proofread the manuscript.

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Competing financial interests

The authors have no conflict of interest.

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