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Opinion

Could A Non-Invasive Biosensor Be Used to Diagnose Alzheimer's Disease?

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Introduction

Alzheimer's Disease (AD) is a precursor to Dementia as the most common subset and contributes to 60-70% of cases [1]. AD diagnosis is a progressive neurodegenerative disease which causes non-reversible impairment to cerebral functioning [2]. It is characterized by symptoms of memory loss, confusion, loss of social functioning and speech and motor deficits [3]. The prevalence and incidence in older people diagnosed with Dementia is that 944,000 people were estimated to be living with Dementia in the UK in 2023 [4]. The costs associated with Dementia care are substantial and currently cost £32,250 per person [5]. The cost to the UK in 2021 was estimated to be £25 billion which is expected to rise to £47 billion by 2050 [1,6]. Developing a non-invasive biosensor, which utilizes a saliva collection method to provide early diagnosis of AD, could streamline the diagnosis pathway, allow more effective treatment pathways for patients, and provide better care options [7].

What are the Current Methods of Detecting Biomarkers for Alzheimer's Disease?

The diagnosis of Alzheimer's Disease, in the first instance, consists of cognitive testing, such as memory, problem solving and language assessments [8]. Then blood, urine and other fluid samples are taken to identify, or rule out, other root causes of the symptoms. Thirdly imaging scans are used; They provide data such as brain atrophy or accumulations of protein-formed plaques indicative of Biomarker prevalence and thus provide diagnosis of AD and its progressive stage. These methods are carried out via imaging scans such as Computerised Tomography (CT), Magnetic Resonance Imaging (MRI) and Positron Emission Tomography (PET) scans. Whilst these scans are effective and accurate, they have limitations including high costs to the healthcare system, with the price of CT and MRI equipment costing between £589,000 to £895,000 per machine [9]. Other limitations include their time-consuming nature and dependence upon access to the equipment and skilled care-workers in a clinical setting which can limit patient access to these resources [10]. Furthermore, MRI is only indicative of later stages of the disease by which time irreversible damage will have occurred [11]. Fluid biomarkers are currently identified in Cerebrospinal Fluid (CSF), via lumbar puncture, which is an invasive and painful procedure. Existing test measures for measuring biomarker proteins, such as Amyloid-beta and Tau, include ELISA (Enzyme-linked immunosorbent assay). This is a test used to measure antibodies, antigens, proteins and glycoproteins in a biological sample [12].

What are the limitations to existing methods of Biomarker detection?

Commercially available biomarker tests, such as Enzyme-Linked Immunosorbent Assay (ELISA), can detect the presence of AD biomarkers [12]. The limitations of these tests are that the results are labour-intensive to obtain; in that a large sample volume (at least 100 µL) is required and the results have been reported to have weak protein-antibody interactions which can lead to undetected results [13]. Detection of Aβ42 in plasma is possible through immunoprecipitation and Liquid Chromatography-Mass Spectrometry (IP-MS), Single Molecule Array (SIMOA), and Immunomagnetic

Reduction (IMR). These methods require expensive resources to obtain results and must be carried out in a laboratory environment [14]. Similarly obtaining Cerebrospinal Fluid (CSF) as a biomarker source has risk of Adverse Effects (AE) such as headaches and pain from the needle-insertion area of the lower spine through Lumbar Puncture [15].

What Existing Solutions Are There to Improve Detection of Alzheimer's Disease?

Current developments in the field of Alzheimer's Disease detection are in development which are quicker, cheaper and less invasive than existing detection methods of brain imaging scans or Lumbar Puncture. A recent discovery by *Ashton, et al*. [16] evaluated a commercially available blood test for AD [16]. The immunoassay identified p-tau217 and produced results which were comparable to using CSF biomarkers, including at preclinical stage [16]. The existing challenges for these tests are to seek validation across platforms at clinical trial stage.

Future Outlook on Wearable Biosensors to Detect AD

Developments in the detection of blood biomarkers for AD are making the likelihood of a wearable biosensor to detect AD a future possibility [16,17]. The push towards developing commercially available assays which detect biological AD in blood, or saliva, would speed up diagnosis time, offer screening functions to the diagnosis pathway, and offer patients more choice in their treatment pathway if diagnosed early [18]. Further developments in the field could be developing a wearable biosensor which utilizes these techniques in a personalized health monitoring function for the user.

Acknowledgments

None.

Conflict of Interest

None.

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