A Psychometric Assessment Method for the Early Diagnosis of Alzheimer's disease

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Abstract— Gerontology deals with the different clinical problems that are common in older people, and some of these follow the traditional system pattern of clinical practice. Patients characteristically have poor insight and often attribute their early symptoms of amnesia to normal ageing. Alzheimer's disease (AD) is common form of senile dementia. There are several causes for the disease. Although our understanding of the key steps underlying neurodegeneration in Alzheimer's disease (AD) is incomplete, it is clear that it begins long before symptoms are noticed by patient. Any disease modifying treatments which are developed are most likely to be successful if initiated early in the process, and this requires that we develop reliable, validated and economical ways to diagnose Alzheimer's type pathology. However, despite comprehensive searches, no single test has shown adequate sensitivity and specificity, and it is likely that a combination will be needed. There are lot of tests and imaging modalities to be performed for an effective diagnosis of the disease. Conventional clinical decision making systems are more manual in nature and ultimate conclusion in terms of exact diagnosis is remote. In this case, the use of advanced biomedical engineering technology will definitely helpful for making diagnosis. Profiling of human body parameter using computers can be utilised for the early diagnosis of Alzheimer's disease. There are several imaging techniques used in clinical practice for the diagnosis of Alzheimer's type pathology. Prominent of them are Magnetic Resonance Imaging Scan (MRI), Positron Emission Tomography (PET) ,Single Photon Emission Computed Tomography Scanning (SPECT) and Optical Coherence Tomography (OCT). Apart from above, in this paper we have developed a psychometric assessment method based on Mini Mental State Examination (MMSE) to find out the current stage of the disease. This method can be very useful as a medical aid as it saves time and money than the conventional method.

Index Terms— Alzheimer Disease (AD), C++ language, Dementia, Diagnosis, MMSE, Modalities, Psychometric.

1 Introduction

THE early diagnosis of Alzheimer's disease (AD) plays important role on preventing the disease at its earlier stage itself [1],[2]. Alzheimer's disease (AD) is an irreversible age related neurodegenerative disorder of the brain that leads to memory loss and impairs the ability to perform routine functions as well [3], [4]. The impairment of normal functions not only affects the patients but the family members as well. Alzheimer's disease was discovered in 1906 by Alois Alzheimer, a German neurologist and psychiatrist [5]. In 2001, eleven million people suffered from Alzheimer's disease worldwide. At present nearly 36 (35.6) million people are believed to be living with Alzheimer's disease or other dementias, increasing to nearly 66 (65.7) million by 2030 and more than 115 (115.4) million by 2050 [6]. The number of people with dementia will increase two fold by 2030, and three fold by 2050 [7], [8]. The advancement of the disease can be divided into three different stages. The first stage is known as Mild Cognitive Impairment (MCI), which do not significantly change daily routine. Between 6 and 25% of people affected with MCI progress to AD every year. The succeeding stages of Alzheimer's disease (Mild and Moderate AD) are characterized by an increase in cognitive impairment, and lowervindependence, culminating in the patient's complete dependence on caregivers and a complete degradation of personality (Severe AD).

Alzheimer's disease is the sixth-leading cause of death and seventy percent common in all cases of dementia [9]. According to another survey, in 71 sec someone I has a tendancy to develop Alzheimer's disease and the rate will increase doublefold every 10 years after the age of 65 [10], [11]. AD is one of the following causes of dementia. Dementia is the frequently used term which indicates cognitive brain functions and follows symptoms like memory degradation, leads to confusion of places and things, not able to complete daily tasks, loss of mental functions and impaired judgment. But, this condition is a symptom of many following brain disorders including Alzheimer's disease, Dementia with Lewy Bodies, Vascular Dementia, Normal-Pressure Hydrocephalus, Parkinson's disease and Frontotemporal Dementia. AD is the most common cause of dementia and is clinically proven that when there is gradual loss of higher mental functions including change in mood,behavior and personality. The symptoms related to AD may leads to orientation problem and difficulty in language, indicating cortical improper functioning, impairment in recognizing object or things and humans, impaired motor function and above all, memory impairment. With the advancement of the disease, patients suffer disability and immobility. The brain structure of AD patients has a total cortical atrophy with enlargement of ventricles [12].

The most significant neuropathological hallmarks of AD are neurofibrillary tangles and senile plaques. Tangles are fila-

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mentous bundles in cytoplasm of the neurons displacing or encompassing nucleus. Senile or neuritic plaques present outside the neuron, appears as a spherical shape bearing dilated neuritic processes around an amyloid beta core which contains some abnormal proteins like amyloid beta plaques which are derived through the processing of Amyloid Precursor Protein (APP) [12]. Genetic mutations or familial causes involved in AD pathology include mutations on chromosomes 1, 14 and 21. Plaques and tangles do occur in normal ageing brains, they are more numerous and more widely distributed in brains of patients with Alzheimer disease. The determination of whether plaques and tangles cause neuronal degeneration or are simply markers of it is essential for designing effective treatment strategies. Although the role of plaques and tangles in AD is still not known precisely, they are found in greatest abundance in the areas of the brain most affected in Alzheimer disease, namely the hippocampus, temporal cortex, frontal cortex and parietooccipital cortex. The hippocampi show the earliest changes in Alzheimer disease and have the highest concentration of plaques and tangles. This finding corresponds to the early and progressive symptoms of memory loss in patients with AD. The development of plaques and tangles in cortical areas correspond to the other clinical findings seen in Alzheimer disease, including abnormal visuospatial orientation, difficulty with skilled tasks and language abnormalities. The progressive loss of neurons and neuronal interconnections, known as synapses, is associated with a decrease in the concentrations of neurotransmitters, the chemical signals that are sent between neurons. One such neurotransmitter is acetylcholine, the decline of which is hypothesized to be one of the factors responsible for the intellectual deterioration seen in both normal ageing and in Alzheimer disease [13]. Other risk factors for this type of disease are advanced age, small head size, history of head trauma, lower intelligence, and female gender [14]. In this paper we have developed a psychometric assessment method based on a clinical test known as MMSE which is used to find the stage of the disease.This has been developed with the help of powerful programming C++ language. This test can be consider as a screening test so that it is useful before diagnosing the disease with help of different imaging modalities. This paper is an extended research work of the previous works that are cited in this manuscript [1], [2], [3], [4].

2 Early Diagnosis of AD

There is increase proof that early diagnosis of Alzheimer disease will be the key factor to get the benefits of better treatment. But frequently, patients are diagnosed in later stages of the disease, when disabling symptoms and neuropathological changes have become well established. At present there is a lack of disease-modifying treatment in the case of AD, inventing sensitive and specific markers of early AD would be a major breakthrough as it would slowdown or arrest the degenerative process before dementia develops. Furthermore, current symptomatic treatments may be more efficiently applied in the initial stages of AD. However, early diagnosis remains difficult to achieve, and currently the clinical diagnosis of AD comes relatively in the advanced stage of the disease. The diagnosis of clinically probable AD can currently be made in living subjects only once the stage of dementia has been reached. It is based on a number of criteria as defined by the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) and the Alzheimer's Disease and Related Disorders Association (ADRDA), but can only be confirmed during autopsy[15]. Some earlier tests that were conducted for AD are neuropsychological tests, Computed Tomography (CT) scans and structural Magnetic Resonance Imaging (MRI). Neuropsychological tests are mainly used for determining the specific type and degree of cognitive dysfunction [16].

CT scans were normally used to look for atrophy of the brain, and enlarged ventricle size. Firstly it was believed that cerebral atrophy was significantly higher in patients with AD than those didn't have. However it was discovered later that healthy people also have cerebral atrophy. Patients with dementia may not have cerebral atrophy at least in the earlier stages of the disease. Therefore, CT scans have been deemed as clinically not useful in the primary diagnosis of AD. After CT, the additional benefits of structural MRI data were introduced. Structural MRI measures the "medial temporal lobe structures, ventricular volumes and whole brain volumes. Therefore MRI can be helpful in differentiating between MCI and AD [17].In addition, Positron Emission Tomography (PET) uses biochemical means of acquiring images rather than structural information. Positron emitting radioisotopes are used to generate the radioactivity". PET scan can measure different compounds in the brain, in the case of AD; PET is used to measure fluorodeoxyglucose (FDG). With dementia patients the neurons intake of glucose and FDG decreases. " By highlighting regions of decreased FDG uptake, PET can theoretically help in the diagnosis of dementia, even if there is absence of the gross structural damage detected by other imaging techniques such as CT or MRI" [18]. Some studies have been conducted to find out dementia patients that are deemed amyloid positive or amyloid negative. Amyloid positive patients are said to be dominant carriers of AD, while amyloid negative patients are not performed this kind of study and they found [18], [19],"amyloid positive subjects with mild cognitive impairment were much more likely to progress to a clinical diagnosis of Alzheimer's disease than amyloid negative subjects with mild cognitive impairment". PET has been used widely to study about AD, and it is evolving into an effective tool for early diagnosis. PET has been used to detect people at risk for AD even before the symptoms start. PET is a very expensive scan to perform although it has been the most

useful as far as providing visual images in the detection of AD. All of these tests can help to show the memory recall of a patient and the possible areas where the patient lacks deficiency. Using these tests can be helpful to find the types of treatment plans that can be given, however neuropsychological tests alone are not helpful in detecting early AD. Trials were then conducted combining neuropsychological tests with clinical tests and various imaging technologies. For an effective and early diagnosis of AD, a population based study is necessary and required, which gives an idea about the various tests involved in determining AD.

In practice, a clinical diagnosis of AD is made when patients have progressive memory decline for over 6 months with a resulting impairment of selfcare and social or occupational functioning. The presence of objective memory impairment should be documented by the Mini-Mental State Examination (MMSE) and other neuropsychological tests. Despite of other neuropsychometric assessment method, in this paper we developed the memory acessment method using the concept of MMSE. We have chosen this method for developing the software because it is very simple and total examination time needs only less than 10 minutes.

3 Mini Mental State Examination (MMSE)

The Mini Mental State Examination (MMSE) is a tool that can be used to systematically and thoroughly assess mental status [20]. It is an 11-question measure that tests five areas of cognitive function: orientation, registration, attention and calculation, recall, and language. The maximum score is 30. A score of 23 or lower is indicative of cognitive impairment. The MMSE takes only 5-10 minutes to administer and is therefore practical to use repeatedly and routinely. The MMSE is effective as a screening tool for cognitive impairment with older, community dwelling, hospitalized and institutionalized adults [28]. Assessment of an older adult's cognitive function is best achieved when it is done routinely, systematically and thoroughly. Since its creation in 1975, the MMSE has been validated and extensively used in both clinical practice and research. The MMSE is effective as a screening method to separate patients with cognitive impairment from those without it. In addition, when used repeatedly this method is able to measure changes in cognitive status that may benefit from intervention [21]. However, this method is not able to diagnose the case for changes in cognitive function and should not replace a complete clinical assessment of mental status. In addition, this method relies heavily on verbal response and reading and writing. Therefore, patients that are hearing and visually impaired, intubated, have low English literacy, or those with other communication disorders may perform poorly even when cognitively intact. In this paper we can overcome the communication problem of those who are virtually impaired [22], [23].

4 Software Used

C++ is a practical and still-current software tool; it remains one of the most popular programming languages in existence, particularly in areas such as embedded systems. C++ facilitates writing code that is very efficient and powerful and, given the ubiquity of compilers, can be easily ported to many different platforms. Also, there is an enormous code-base of C++ programs developed over the last 30 years, and many systems that will need to be maintained and extended for many years to come. The second key objective is to introduce the basic concepts of software design. At one-level this is C-specific: to learn to design, code and debug complete C++ programs. At another level, it is more general: to learn the necessary skills to design large and complex software systems. This involves learning to decompose large problems into manageable systems of modules; to use modularity and clean interfaces to design for correctness, clarity and flexibility [24].C++ is a gen eral-purpose programming language, and is used for writing programs in many different domains, such as operating systems, numerical computing, graphical applications, etc. It is a small language, with just 32 keywords. It provides "high level" structured programming constructs such as statement grouping, decision making, and loping as well as "low level" capabilities such as the ability to manipulate bytes and addresses. C++ achieves its compact size by providing spartan services within the language proper, foregoing many of the higher-level features commonly built-in to other languages, there are no memory management facilities apart from static definition and stack-allocation of local variables. And there are no input/output facilities, such as for printing to the screen or writing to a file. Much of the functionality of C++ is provided by way of software routines called functions. The language is accompanied by a standard library of functions that provide a collection of commonly used operations [25]. A C++ program, whatever its size, consists of functions and variables. A function contains used during the computation statements that specify the computing operations to be done, and variables store values C++ is a typed language. Each variable is given a specific type which defines what values it can represent, how its data is stored in memory, and what operations can be performed on it. By forcing the programmer to explicitly define a type for all variables and interfaces, the type system enables the compiler to catch type-mismatch errors, thereby preventing a significant source of bugs. There are three basic types in the C language: characters, and integer and floating-point numbers. The numerical types come in several of sizes. In this paper we have developed psychometric assessment software with the help of C++ language as it is a powerful tool to analyse and compare the different aspects of MMSE. For the execution of this method we have use the Turbo C++ 4.0 Windows 7 Windows 8 64Bit Version.

5 Implementation and Results

As we have used the C++ language, we have made the psychometric assessment method as an executable file which can used in windows as well as other platform. The memory space required for the Turbo C++ 4.0 Windows 7 Windows 8 64Bit Version is 2.01 kb. By this version of C++ we have executed as an application with .exe file. The total size of this application is about 32 kb. Therefore the memory required for this file is very low. The MMSE questionnaire [26] implemented using C++ language can be summarised as in a table 1 as shown below.From the table it shows the four conditions of the patient with dementia and its range of values. Also we can interpret the MMSE scores as in table 2. The application that we developed can be used as an executable file in any platform. Also it assists the physicians in their diagnosis.

scores	condition
24 – 30	Normal
18 – 23	Mild dementia
10 – 17	Moderate dementia
<10	Severe Dementia

Table 1: MMSE score

Degree of Impairment	Score	Psychological Assessment	Routine function
Mild	18-23	Help to determine pattern and extend of deficits	Significant effect. May require some supervision,support and assistance
Moderate	10-17	Formal assessment may be helpful if there are specific clinical indications	Clear impairment. May require 24hr supervision
Severe	0-10	Patient not likely to be testable	Marked impairment. Likely require 24 hour supervision

Table 2: Interpretation of MMSE scores

8. Conclusion

There are a lot of clinical tests, drug therapies and diagnostic tools such as biomarkers and neuroimaging techniques are available for the diagnosis of Alzheimer's disease. But the fact is that these techniques are inadequate for the definite diagnosis at the earlier stages. So this software can be used as a reliable and efficient method before diagnosing the disease without going to a critical stage. This software can be used in conjunction with the advanced Biomedical Engineering technology using the aid of other clinical tests, neuroimaging techniques such as SPECT, MRI, PET, OCT etc, databases such as ADNI, OASIS etc and soft computing tools. In the future with the combination above said tests we can make a complete expert system for the early diagnosis of AD.

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