

**Designing a tool for early diagnosis for dementia from neuroimaging data using machine learning**

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# Abstract

# Acknowledgment

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# Introduction

## Dementia

Dementia is a cumulative term for a variety of changes that affect brain physiology, those effect person’s daily activities by causing long term and often progressive diminishing on capability of thinking and remembering. In addition to these symptoms, there are emotional disturbances, difficulty on speech and motivational decrease (Burns and Iliffe, 2009). On diagnosis there should be distortions on person’s mental functioning and one expected to have a significant decrease than projected due to aging (Budson et al., 2016). Until late 19th century, dementia had a vague description and a simple clinical concept, that at that time it can described as anyone who had lost their ability to think and reason, and according to that time it also includes the mental illnesses and incapacities those can be reversible by right treatment (Berrios, 1987). As some studies state that there is no known cure for dementia, however there are some medication that could help people where disease is at mild to moderate stage, but overall expectation of positive feedback is unlikely (Comission de la transparence, 2012). In the study which Zaccai et al conducted which was investigating the conducted studies on population-based experiments, they are offering that these studies could break the existing walls on biological indicators of cognitive and behavioral changes that comes with aging, and could provide further details with their wide variety of clinical and neuropsychological information (Zaccai et al., 2006).

### Epidemiology

Dementia cases’ number was estimated as 35.6 million in 2010 worldwide, and two thirds of this population lays on low and middle income countries (Hendrie et al., 2004). Population in the Earth is growing old, because of that dementia had become one of the biggest concerns globally, which causes a significant burden for the people themselves besides their families and social and health care groups (Prince et al., 2014). Estimated population with dementia is projected to be 135 million within 2050, and the cost of care calculated as $604bn globally in 2010 and it is expected to rise around $1tr by 2050 (Prince et al., 2014). Iliffe et al. states that belief amongst professionals that is the lacking of the cure which does not help any patient with diagnosed dementia, causes delays on the diagnosis part (Iliffe et al., 2009). In the population of patients who are suffering from dementia, vast majority of them are diagnosed with Alzheimer’s disease, followed by vascular dementia and Lewy body dementia, to provide the rates out of 10-15 thousand patients 5-8 thousand of them are suffering from Alzheimer’s disease (Bermejo-Pareja et al., 2008). Another study carried out that 0.4% of world’s total population is afflicted by Alzheimer’s in 2006, to be more precise absolute number is 26.6 million, and with its growing rate, people’s extended life time could be a factor on it, currency of AD would be three times bigger and the exact number of people inflicted to be quadrupled by 2050 (Brookmeyer et al., 2007).

### Alzheimer’s disease

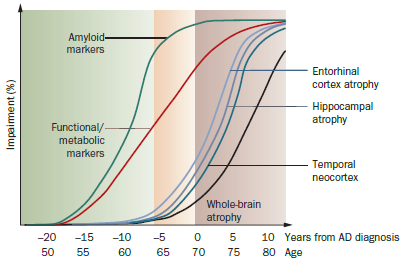
Alzheimer’s disease is a neuro-degenerative disorder, which has effects on the areas of the cerebral cortex and hippocampus, and is progressive and unremitting, first symptoms are usually spotted in the brain tissue that contains frontal and temporal lobes then it spreads to the other areas of the cortex and progression of the disease varies between individuals (Masters et al., 2015). The disease is the rapid failure of the amyloid- β (Aβ) peptide from the inner sections of the brain, which is a chronic illness, contains preclinical and prodromal phases those took approximately 20 years (Golde et al., 2000). Rate of the disease diagnosed amongst the population with the age over 65 years old is 10-30% (Bachman et al., 1993). The disease shows sporadic form on the 95% of the patients, which means it progresses and spreads exponentially within the brain cells. The disease is related with the accumulation of forms of amyloid-β those are insoluble in plaques in extracellular spaces, as much as in plaques in the walls of blood vessels, and the aggregation of the microtubule protein those are in neurofibrillary tangles in neurons (Spielmeyer et al. 1922). Average duration of the sickness is approximately 8-10 years, yet the clinical phases those have the symptoms are followed by the stages those were mentioned before, are preclinical and prodromal, which extends the duration over two decades (Evans et al., 2003). Sporadic type of Alzheimer’s disease is the most frequent which has an age of onset of 80 years (Masters et al., 2015). The main issue is brain tissue cannot be cleansed from Aβ peptide. At the other hand, co-morbidies (i.e. cerebrovascular disease) and hippocampal sclerosis are very common at this age, which makes diagnosis really complicated, in addition to that Alzheimer’s disease have many characteristics in common with other molecularly defined neuro-degenerative diseases, for example Parkinson’s disease (Duncan et al., 2014). With all the symptoms and the progress of sickness brings one question upfront, which is Alzheimer’s disease is a normal part of aging or it is a discrete disease process.

#### Patophysiology

#### Diagnosis and Monitoring

Making a diagnosis of Alzheimer’s disease is really challenging, because in the prodromal stage patients have not only subtle cognitive symptoms, as they also are in the dementia phase (Knopman et al., 2001). That causes misdiagnoses clinically (%35), that patients with negative Aβ PET scans were misdiagnosed as having Alzheimer’s disease, and also co-morbidies and hippocampal sclerosis aid to the difficulty of the judgement (Salloway et al., 2014). In England, there was a study introduced to find the cases who are in the high risk group such as people older than 75, with that said age is the most significant factor for dementia, and people with high vascular risk, Parkinson’s disease and learning impairment which were effected either in wrong way or right way by the policy (Bamford et al., 2007). The policy emphasized memory assessment of people who may or may not have the symptoms, which raised the stress of the patients and questioned itself as it is cost effective (Iliffe et al., 2009). As stated before diagnosing either dementia and Alzheimer’s disease can be difficult due to subject not accepting that he/she forgets at their earlier stages, symptoms’ similarity with memory loss that comes with normal ageing process and diversity of other indications as well, for example uncertainty on making decisions and hassle to find the words whilst speaking (Kostopoulou et al., 2008).

Aβ PET imaging contains a technique (Pittsburgh compound B (PiB)) that uses radioactive analogue of the fluorescent amyloid dye thioflavin-T, which goes through the barrier between blood and brain, binding Aβ (Mathis et al., 2002). In the past ten years studies with PiB helped people radically to understand the correlation between Aβ accumulation and cognitive decline and neuro-degeneration at the preclinical, prodromal and dementia phases of Alzheimer’s disease. The studies show that deposition of Aβ starts years before dementia and being followed by cognitive decline and brain atrophy, and also in long term studies Aβ PET is a significant marker on forecasting the progression from mild cognitive impairment to dementia, caused by Alzheimer’s disease (Rowe et al., 2013, Villemagne et al., 2013). Hippocampal volume is measured by the neuronal counts, in early, mild stages of AD Hippocampal volume is already decreased 15-30% whereas, in a converting type of Mild Cognitive Impairment which turns into Alzheimer’s disease on later stages, the volume is decreased by 10-15% (Shi et al., 2009). However, atrophy values vary with the progression of the severity of AD, in contrast as shown in Figure 1 Aβ markers are more likely to be effected than structural markers to conversion of MCI to mild stages of AD (Sluimer et al., 2008).



**Figure 1: Difference the changes between the biomarkers during the advance of Alzheimer’s disease.**

Theoretical model of biological markers in Alzheimer’s disease, green parts are the stage that there are no symptoms exist whereas, orange part indicates mild cognitive impairment and brown part is where all the samples are diagnosed with Alzheimer’s disease. Figure is obtained from Frisoni et al. (2010).

## Image processing on Diagnosis

# Objective

# Methods

## Data Handling

### Use of Big Data Techniques

## Image Processing

### Brain Segmentation

### Add all the other image processing methods here

## Machine Learning

### Support Vector Machine

### Add all the other machine learning techniques here

# Results

## Results for each methods used

## Method 2

# Discussion

# Conclusion

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