ALZHEIMER'S DISEASE PROGRESSION ANALYSIS AND CLASSIFICATION USING T_1-WEIGHTED MRI

By

Basma Hassan Ahmed Ali

A Thesis Submitted to the
Faculty of Engineering at Cairo University
in Partial Fulfillment of the
Requirements for the Degree of
MASTER OF SCIENCE
in
Biomedical Engineering and Systems

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Title of Thesis: Alzheimer's Disease Progression Analysis and Classification for T_1-Weighted MRI

Key Words:
Alzheimer's disease; MRI; MMSE; SVM; VolBrain

Summary:
Alzheimer's disease (AD) is a considered one of the common elderly diseases. It is a type of dementia that causes changes in behavior in addition to memory loss because of the death of brain cells. There are three stages for Alzheimer disease named: Alzheimer's Disease patient (AD), Mild cognitive impairment (MCI) and Early stage. In this work, we proposed a promising method to classify the different categories of Alzheimer and the healthy control (HC) subjects using multiple T_1-weighted MRI scans of the whole brain volume directly to extract several features by subtracting the longitudinal data of different visits and compute the associated changes in the brain. These features are then fed to the Support Vector Machine (SVM) classifier. The main advantage of this method is that it doesn't involve lots preprocessing steps including the segmentation that was done to extract the hippocampus or amygdala or any other region of interest, which is considered as an expensive and complicated process. The second part of this thesis is employing a bio-statistical anaylsis to compute the cross-sectional correlation/regression between different clinical assessments such as MMSE,… and … and four Volume of Interest (VOI) named hippocampus, amygdala, lateral ventricles and total brain volume formed of WM and GM. It was observed that MMSE is the most significant assessment, having a high correlation with the four VOI. The graphical representation of the volumetric changes in the different VOI was studied longitudinally along with the shrinkage rate of hippocampus, amygdala and overall brain volume as well as the enlargement rate of lateral ventricles through the progression stages of the disease compared to the normal subjects.

Disclaimer

I hereby declare that this thesis is my own original work and no part of it has been submitted for a degree qualification at any other university or institute.

I further declare that I have appropriately acknowledged all sources used and have cited them in the reference section.

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First and foremost, I thank **ALLAH**, the most gracious, the ever merciful for helping me finishing this work. I want to thank all those, who helped me by their knowledge and experience. I will always appreciate their efforts. I would like to offer my sincere thanks to **Dr. Mustafa El-Attar** for his cooperation and support and my supervisors **Prof. Dr. Ayman Eldeib** and **Assoc. Prof. Dr. Inas A. Yassine.** I owe them for valuable supervision, continuous encouragement, useful suggestions, and active help during this work. My sincere appreciation and gratitude to my family for their help and patience during the preparation of this work

Table of Contents

List of Tables

List of Figures

Nomenclature

AAL	Automated Anatomical Labeling
AD	Alzheimer’s disease
ADNI	Alzheimer's disease Neuroimaging Initiative
ANOVA	Analysis of Variance
BET	Brain Extraction Tool
BOVW	Bag-of-Visual-Words
CDR	Clinical Dementia Rating
CHF	Circular harmonic functions
CT	Computed Tomography
CSF	Cerebrospinal Fluid
DL-CNN	Deep Learning- Convolutional Neural Networks
EM	Expectation and maximization
EEG	Electroencephalography
FAQ	Functional Activities Questionnaire
FMRI	Functional Magnetic Resonance Imaging
FSL	FMRIB Software Library
GDSCALE	Global Deterioration Scale
GM	Gray Matter
GUI	Graphical user interface
HC	Healthy Control
IADL	Instrumental activities of daily living
ITK	Insight Segmentation and Registration Toolkit
KNN	K-nearest neighbor classifier
LDA	Linear discriminant analysis
LOOCV	Leave One Out Cross Validation
MCI	Mild cognitive impairment
MLE	Maximum likelihood estimate
MMSE	Mini Mental State Examination
MRI	Magnetic Resonance Imaging
NIA	National Institute on Aging
NIBIB	National Institute of Biomedical Imaging and Bioengineering
NTI	Normalized Thickness Index
OPLS	Orthogonal Partial Least Squares to Latent Structures.
PCA	Principle component analysis
PCC	Posterior cingulate cortex
PET	Positron emission tomography
RBF	Radial Basis Function
ROC	Receiver Operating Curve
ROI	Region of interest
TIV	Total Intracranial Volume
SIFT	Scale-invariant feature transform
SPECT	Single-photon emission computed tomography
SPHARM	Spherical harmonics
SPHARM-PDM	Spherical Harmonics-Point Distribution Model

SPM	Statistical Parametric Mapping
SURF	Speeded-Up Robust Features
SVM	Support vector machine
SVM-RFE	SVM Recursive Feature Elimination
VBM	Voxel-based Morphometric
VOI	Volume of interest
VolBrain	Volume of Brain
WM	White Matter

Abstract

Alzheimer’s disease (AD) is a considered one of the common elderly diseases. It is a type of dementia that causes changes in the patient behavior in addition to memory loss because of the death of brain cells. It is considered a chronic neurodegenerative progressive disease which gets worse over time. In the Early stage, the patient may perform his/her usual activities as he/she still drive, work and deal with other people but with less efficiency. Later occurs the Mild Cognitive Impairment (MCI) stage, known as moderate Alzheimer's disease, that is considered the longest stage and may last for many years in which the patient may suffer from many troubles like confusing words, getting frustrated or angry, or acting in unexpected ways. AD, is the severe stage or late stage, where the patients lose their ability of responding to their usual environment and that ends with the patient death.

The Hippocampus and Amygdala regions, subregions of the limbic system, are very good indicators for the presence of AD and considered as the most affected part in terms of shape and volume by the Alzheimer deterioration since they are responsible for the memory storage. Moreover, In Alzheimer's disease, there is an overall shrinkage of brain tissues in addition to enlargement of the lateral ventricles.

There is no single medical test that proves a person has Alzheimer's. Diagnosing Alzheimer's involves a complete assessment that is formed of few tests such as : Mini Mental State Examination (MMSE) and Clinical Dementia Rating Scale (CDR), as the standard dementia screening and staging severity tests. There are also other clinical assessments that are used such as The Functional Activities Questionnaire (FAQ) and The Global Deterioration Scale (GDSCALE). These four assessments are based on a scoring system.

In this work, we propose a promising method to classify the different categories of Alzheimer and the healthy control (HC) subjects using a series of longitudinal T_1-weighted MRI scans of the whole brain volume for every follow-up visit. The difference volume of each visit is computed by subtracting each follow-up scan from the baseline MRI to get the 3D feature vector associated with every subject. These features are then fed to the decision support system. The main advantage of the proposed system is eliminating most of the preprocessing steps, which in its turn decreases the processing time and though the overall cost in terms of time and cost. The preprocessing module is formed of the alignment of the longitudinal dataset to the Atlas as well as the down sampling of the volume in order to decrease the processing time.

Both of Two sample T-Test and Fisher Score are studied for dimensionality reduction purposes to overcome the overfitting problem followed by SVM classifier for the classification between HC and MCI subjects, HC and AD subjects and MCI and AD patients. Leave one out cross validation (LOOCV) and 10-Fold are used to study the system robustness based on the accuracy.

The second part of this thesis is employing a bio-statistical anaylsis to compute the cross-sectional correlation and regression model between different clinical assessments such as MMSE,… and … and four Volume Of Interest (VOI) named hippocampus,