THE REPUBLIC OF TURKEY
BAHCESEHIR UNIVERSITY

PREDICTING ALZHEIMER'S DISEASE USING ADAPTIVE NEURO FUZZY INFERENCE SYSTEM

Master's Thesis

ONUR ÇIKRIKÇILI

ISTANBUL, 2013

THE REPUBLIC OF TURKEY
BAHCESEHIR UNIVERSITY

GRADUATE SCHOOL OF NATURAL AND APPLIED SCIENCES
INFORMATION TECHNOLOGIES

PREDICTING ALZHEIMER'S DISEASE USING ADAPTIVE NEURO FUZZY INFERENCE SYSTEM

Master's Thesis

ONUR ÇIKRIKÇILI

Supervisor: PROF. DR. ADEM KARAHOCA

ISTANBUL, 2013

THE REPUBLIC OF TURKEY
BAHCESEHIR UNIVERSITY

GRADUATE SCHOOL OF NATURAL AND APPLIED SCIENCES
INFORMATION TECHNOLOGIES

Name of the thesis: Predicting Alzheimer's Disease Using Adaptive Neuro Fuzzy Inference System
Name/Last Name of the Student: Onur ÇIKRIKÇILI
Date of the Defense of Thesis: 30.07.2013

The thesis has been approved by the Graduate School of Natural and Applied Sciences.

Assoc. Prof. Dr. Tunç BOZBURA
Graduate School Director
Signature

I certify that this thesis meets all the requirements as a thesis for the degree of Master of Science.

Prof. Dr. Adem KARAHOCA
Program Coordinator
Signature

This is to certify that we have read this thesis and we find it fully adequate in scope, quality and content, as a thesis for the degree of Master of Science.

Examining Committee Members	Signature
Thesis Supervisor Prof. Dr. Adem KARAHOCA	----------
Member Assist. Prof. Dr. Alper TUNGA	----------
Member Assist. Prof. Dr. Yalçın ÇEKİÇ	----------

ACKNOWLEDGEMENTS

I express sincere appreciation to my thesis advisor Prof. Dr. Adem KARAHOCA for guiding and facilitating my research activities.

My sincere thanks to Asst. Prof. Dr. Yücel Batu SALMAN and Instructor Tamer UÇAR whom answered my endless questions and inspired me during my research.

I will always be grateful to Prof. Dr. Hakan GÜRVİT and M.D. Başar BİLGİÇ since they let me research with them.

Lastly, but far from least I would like to express my sincerest gratitude to my family, especially to my brother M.D. Uğur ÇIKRIKÇILI who constructed the thesis's medical background. Without his guidance and persistent help this thesis would not have been possible.

Onur ÇIKRIKÇILI

ABSTRACT

PREDICTING ALZHEIMER'S DISEASE USING ADAPTIVE NEURO FUZZY INFERENCE SYSTEM

Çıkrıkçılı, Onur

Information Technologies

Thesis Supervisor: Prof. Dr. Adem KARAHOCA

August 2013, 40 Pages

Alzheimer's disease (AD) one of the major health problem all around the world and unmitigated cure has not been found yet. A correct diagnosis of AD can be affirmed by histopathologic tests. In addition, mental tests and daily activities can lead diagnose of patients' mental condition. The goal of this study is to develop a data mining solution using neuropsychological test results that makes diagnosis of AD and its stages as accurate as possible and assist to medical doctors' final decision.

In this study, Sugeno-Type adaptive-network-based fuzzy inference system (ANFIS), multilayer perceptron (MLP), Iterative Dichotomiser 3 (ID3) and One Rule (OneR) algorithms were assessed whether to could predicting AD. The data set is collected from 264 patients who complained about their health problems and applied to Istanbul University's Department of Neurology. All of the subjects' ages are 65 or over. The blind data records has 11 attributes that covers basic demographic information and neuropsychological test results. Using "Information Gain" filter, ineffective attributes are eliminated.

According to the results, ANFIS classified the instances with the highest correctness rate which is %96 and MLP classified an accuracy of 87%, ID3's is 76% and OneR's is 76%. In addition ANFIS has a high performance based on the methods that sensitivity, specificity and root mean square error.

Keywords: Alzheimer's disease, Prediction of Alzheimer's disease, Dementia, ANFIS, Data Mining

ÖZET

ALZHEIMER HASTALIĞININ UYARLANMIŞ NEURO FUZZY SONUÇ ÇIKARIM SİSTEMLERİYLE ÖNCEDEN TAHMİN EDİLMESİ

Çıkrıkçılı, Onur

Bilgi Teknolojileri

Tez Danışmanı: Prof. Dr. Adem KARAHOCA

Ağustos 2013, 40 Sayfa

Alzheimer hastalığı günümüzün en önemli sağlık sorunlarından biri olup, bu hastalığın tam anlamıyla tedavisi günümüz şartlarında mümkün değildir. Bir hastaya Alzheimer teşhisi koymak için histopatolojik testlere ihtiyaç duyulmaktadır. Buna ek olarak zihinsel testler, günlük aktivitelerinin değerlendirilmesi de hastalığın teşhisinde önemli rol oynamaktadır. Bu çalışmanın amacı, hastaya uygulanan nöropsikolojik testlerin sonuçları doğrultusunda veri madenciliği çözümü geliştirmektir. Böylece hekimlerin Alzheimer teşhisinde hız kazanıp hastalık hakkındaki kararlarında kolaylık sağlaması amaçlanmaktadır.

Bu çalışmada, Alzheimer hastalığının önceden tahmini için, Sugeno-Type adaptive-network-based fuzzy inference system (ANFIS) sistemi kullanılmış, multilayer perceptron (MLP), Iterative Dichotomiser 3 (ID3) ve One Rule (OneR) algoritmaları ile de karşılaştırılmıştır. Tahmin sistemi için kullanılan veriler, İstanbul Üniversitesi Nöroloji Departmanı'na sağlık sorunlarıyla başvuran 65 yaş üstü 264 hastanın kayıtlarından alınmıştır. Kayıtlar, hastaların demografik özellikleri ile birlikte, nöropsikolojik testler sonuçlarından oluşan 11 temel özellikte gruplanmıştır. Bir sonraki aşamada işlevsel özelliklerin kullanılması için "Information Gain" filtresi ile veriler filtrelenmiştir. Filtreleme sonucu, yaş ve cinsiyet çıkarılarak bu sayı 9'a düşürülmüştür.

Yapılan çalışmalar neticesinde ANFIS verileri 96% oranında hastanın gruplandırılmasını doğru olarak hesaplamıştır. MLP algoritması 87%, OneR ve ID3 algoritmaları da 76% oranında başarı göstermiştir. Aynı zamanda hassaslık, özgünlük ve ortalama karesel hata değerlerinde ANFIS'in diğer algoritmalara göre belirgin bir şekilde daha iyi performans sergilediği gözlemlenmiştir.

Anahtar Kelimeler: Alzheimer hastalığı, Alzheimer hastalığının tahmini, Bunama, ANFIS, Veri Madenciliği

CONTENTS

TABLES

FIGURES

ABBREVIATIONS

AD	:	Alzheimer’s disease
ADRDA	:	Alzheimer’s disease and Related Disorders Association
ADNI	:	Alzheimer's disease Neuroimaging Initiative
ANFIS	:	Adaptive – Network - Based Fuzzy Inference System
BDRS	:	Blessed Dementia Rating Scale
BIMC	:	Blessed Information-Memory-Concentration
BOMC	:	Blessed Orientation – Memory – Concentration
CDR	:	Clinical Dementia Rating
CDR - SB	:	Clinical Dementia Rating – Sum of Boxes
FDG - PET	:	Fluorodeoxyglucose Positron-emission tomography
FN	:	False Negative
FP	:	False Positive
GDS	:	Global Deterioration Scale
GerDS	:	Geriatric Depression Scale
ID3	:	Iterative Dichotomiser 3
MAPS	:	Multi Atlas Propagation And Segmentation
MCI	:	Mild Cognitive Impairment
MLP	:	Multilayer Perceptron
MMSE	:	Mini-Mental State Examination
MRI	:	Magnetic Resonance Imaging
NINCDS Stroke	:	National Institute of Neurological and Communicative Disorders and
OneR	:	One Rule
PET	:	Positron-emission tomography
POSAD	:	Possible Alzheimer
PRAD	:	Probably Alzheimer
RMSE	:	Root Mean Squared Error
SPECT	:	Single Photon Emission Computed Tomography
TN	:	True Negative
TP	:	True Positive

1. INTRODUCTION

1.1 PROBLEM DEFINITION

Alzheimer's disease (AD) is probably the most common dementia model of today's modern society which described as eponym disease in 1906 by Alois Alzheimer. Macro / microscopic findings was documented from his famous patient Auguste D. Researches show that (Brookmeyer et. al. 2007) according to the prevalence rates, this irreversible neurodegenerative disease becomes one of the most important public health problem. AD has 6.4 percentage rate in all over 65 year old society. Also women have mildly elevated risk than men but yearly incidence risk is coequal within two genders and it is the most common dementia disorder in society (65 percent of all dementia syndromes). Studies demonstrate that hypertension, cholesterol, lack of social networks, diabetes (generally vascular risk factors), head trauma, having a 1st degree relative who has diagnosed AD, education, loneliness and other factors increase the risk of AD (Bennett et. al. 2006; Wilson et. al. 2007; Kivipelto et. al. 2006). This neurodegenerative disease impairs one's mental functions and this impairment accelerates faster and continues during several years before death. In the final phase of AD makes the patient completely immobilized and mentally impaired. The consequences of the disease not only affect the patients but also their families according to the economic and physiological.

AD's clinical symptoms didactically separated in three areas: Cognitive, behavioral signs and daily living activities. Cognitive symptoms and findings are insidious low progressive amnesia, articulation disorders such as anomic aphasia, attention deficits, impaired insight, visio-spatial orientation disorders and executive syndrome deficits. Behavioral symptoms are personality change, delusions (paranoid / persecution delusions), visual hallucinations, Capgras syndrome and sleeping disorders. Daily living activity changes are personal hygiene deficits, calculation problems in dealing, wish / grace missing in hobbies, communication disorder in family and lack of ability in job are can be counted.
By the clinic-pathologic explanation AD is a neurodegenerative disease which characterized progressive-selective neuronal loss. This neuronal lack starts typically in lymbic system and entorhinal cortex. Paralymbic, uni / heteromodal association cortex,

primer sensory and motor cortex areas additionally effected during the progression. Cytologic investigations showed that degeneration's principle reasons are amyloid plaques in intercellular area and hyperphosphorile tau tangles in intracellular side. Histopathological changes such as senile plaques, neurofibrillary tangles, neuropil threads are main characteristics of the disease. In AD, nerve cells that also called neurons die or their functions don't work properly. Loss of neurons cause lack of communication between afferents and efferents of entorhinal cortex and hippocampus. So this fatal disease's symptoms start with deterioration of remember new information and loss of cognitive abilities. Progressive memory loss, lack of ability for doing daily activities, speech, mood and behavioral disorders should be seen during the progression of AD.

There are three well-known types of AD. Early-onset AD one of the rare form of the disease. Generally people whom age is below 65 and have an AD considered as an early-onset AD. Researches (Ashford and Mortimer 2002) show that APOE ε4 allele increased the AD heritability up to 50 percent. Also, APP gene on 21^{th}, Presenilin 2 gene on 1^{th} and Presenilin 1 gene on 14^{th} chromosome is considered findings in autosomal dominant inherited early-onset AD patients. In addition people who have "Down Syndrome" are especially at risk for early-onset AD. Having a Down syndrome diagnosed baby under 35 year old in women, AD risk evaluates 5 flat above. But there is no risk for paternal side. Interestingly, Down syndrome causes early diagnosed AD generally under age 50. The other form of AD is Familial AD. This type of AD known as an inherited AD and at least two members of family have had AD to diagnose as familial AD. It is also the rarest form of AD. The last one is late-onset AD that is the most common form all over the world. Diagnosed people whom age is 65 or more are considered as a late-onset AD. In this research, target subjects are chosen from late-onset group. The advanced consideration about the late-onset group and its effects are done in materials and methods section.

1.2 BACKGROUND

Physicians must need two *sine qua non* (an essential or indispensable element) items to diagnose AD. Detailed *anamnesis* (the medical history of a patient) from patient's relatives and mental examination / neuropsychological tests which prospered for patient's education and social statue. Although there is no essential treatment for AD, with some pharmacological progress, AD's development phases can be abated. In this case, early detection has a highly important role according to the aspects of patient's health and disease's pervasiveness. According to the Alzheimer's Disease Neuroimaging Initiative (ADNI) (Weiner et. al. 2012), there are considerably variety ways to early detection of AD's symptoms using clinical, imaging, genetic and biochemical biomarkers. Positron-emission tomography (PET) (Ikonomovic et. al. 2008) and alternative's is single photon emission computed tomography (SPECT) (Clark et. al. 2008) and fluorodeoxyglucose PET (FDG - PET) (Del Sole et. al. 2008) are popular methods. In addition magnetic resonance imaging (MRI) and its methods functional MRI (Sluimer et. al. 2008), multi atlas propagation and segmentation (MAPS) (Leung et. al. 2010) are also widely known ways for prediction. Gene expression changes (Walker et. al. 2004) and try to find risky genes (Myers and Goate 2001) are also another approaches that analyze the AD from genes factor. CSF biomarkers like β-amyloid quantity and tau / hyper-phosphorylated tau ratio in CSF, and clinical tests (Frisoni and Weiner 2010) are commonly used. Biochemical parameters like vitamine B12, folic acide, homocystein quantity,thyroide hormone level, sphilis and HIV panel is used for differential diagnose. Generally these classification methods are based on machine learning algorithms. From supervised learning support vector machines algorithms to unsupervised tree algorithms variety of way are exist to analyze the image and build a classifier to predict AD.

While popular neuroimaging techniques deals with histopathologic data's of AD, computerized or paper based neuropsychological tests can give an idea about the possibility of being AD and its type. Researches (Fowler et. al. 1997) show that, analysis of two computerized neuropsychological tests, classifies the early dementia with the considerable enough correction rates. Another research state that (Ashraf et. al. 2010) using information gain and Adaptive-Network-Based Fuzzy Inference System (ANFIS)

can be a highly informative guide and diagnose breast cancer with higher accuracy. In the light of these information, goal of this research is compare the ANFIS and other algorithms' accuracy with respect to prediction of patient's possible AD group using seven paper based neuropsychological test results. Hence, in this study, seven paper based neuropsychological test results and demographic data of 264 potential AD patients whom ages is 65 or older are collected, filtered them and lastly classified the subjects to proper groups according to fuzzy logic and other algorithms.

2. MATERIALS AND METHODS

2.1 PREPARING AD DATA SET

For the purpose of the obtain the best prediction model for the AD, data set is collected from Department of Neurology, Faculty of Medicine, Istanbul University, Turkey. The data set covers examination reports of subjects who were examined between January 2008 and September 2012. As listed in Table 2.1, data set is segmented into four different classes using to the criteria for the AD that was established by the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) and the Alzheimer's disease and Related Disorders Association (ADRDA) work-group in 1984 (McKhann et. al. 1984).

2.1.1 Output Classes

In order to the criteria, definite Alzheimer's disease requires histopathologic confirmation, so definite Alzheimer's disease criteria is not added to Table 2.1 due to requirements of histopathologic clinical studies. The other outputs Possible Alzheimer (POSAD), Probably Alzheimer (PRAD) represent the probability of the AD's. In addition, Mild Cognitive Impairment (MCI) also added to table. MCI describes a state that between inevitable aging symptoms and dementia. It is used to describe the subjects whom their cognitive functions are impaired but not fairly enough to call their disease as a dementia. It is also called as the prodromal state of AD (Dubois 2010) due to studies which confirm that between 10 – 15 percent of MCI patients' disease evaluate to AD yearly (Petersen 2009). According to the studies (Gauthier 2006, Nordlund 2005), MCI's prognosis can be diverges, patient's diseases may remain constant or improve. Once and for all, class name "Normal" is added to the table to describe the subjects whom their diseases not considered as a dementia or prodromal state of AD. As seen in Table 2.1, the data set covers the subjects whom are regrouped as 92 of them normal, 55 of them MCI, 57 of them PRAD and lastly 60 of them PosAD.

To prepare the data for ANFIS, these four categorization type is converted to decimal numbers, between 0 and 1, according to the link between the condition and correct diagnosis of AD. Respectively, "Normal" is converted to 0.1; "MCI" converted is converted to "0.5"; "PRAD" is converted to "0.7" and "PosAD" is converted to "0.9".

Table 2.1: Classes for the output variable

Class name	Description	Number of subjects
Normal	Subjects who are not diagnosed as any kind of mental disorder	92
MCI	Subjects who are diagnosed as any kind of MCI	55
PRAD	Subjects who are diagnosed as PRAD	57
PosAD	Subjects who are diagnosed as PosAD	60

2.1.2 Demographic Data

Attributes of the data set can be considered into two groups as follows: demographics data and clinical data. In demographics data, the gender parameter indicates whether the patient is male or female. For ANFIS classification male subjects classified as a zero (0) and females as a one (1). To describe education parameter K12 scale is used which describes from kindergarten to end of secondary education level. Subjects who are illiterate or education level's from kindergarten to end of primary school are classified as a primary education, from end of primary school to end of high school are classified as a secondary education and lastly, people who have undergraduate or higher degree are classified as a higher education. To convert to numeric types for ANFIS, primary education is classified as an education level 1, secondary education is classified as an educational level 2 and lastly higher educational level is classified as an educational level 3. Mean ages (± SD) are 76.56 ± (6.57) for women, 77.12 ± (5.96) for men and 76.85 ± 6.25 for all subjects. The other characteristics of data can be shown in Table 2.2.

Table 2.2: Demographic features and educational status

	Women	Men	Total
Mean age (years)	76.56 ± (6.57)	77.12 ± (5.96)	76.85 ± (6.25)
70 - 74	61	60	121
75- 79	32	63	68
80+	32	43	75
Total	125 (47.34%)	139 (52.66)	264
Mean years of education	6.88 ± (3.38)	7.02 ± (3.8)	6.96 ± (3.6)
Illiterate	22 (45.83%)	26 (54.17%)	48
Primary Education	47 (48.45%)	50 (51.55%)	97
Secondary Education	50 (51.02%)	48 (48.98%)	98
Higher Education	6 (28.57%)	15 (71.43%)	21

2.2 NEUROPSYCHOLOGICAL TESTS

Clinical Neuropsychology verifies the cognitive and behavioral reflections of the mental disorders. It evaluates between brain and higher cortical activity by some evaluation techniques like qualitative observations, neuroimaging findings, analyzing subject's history, and mainly with neuropsychological tests. In below, neuropsychological tests that are used in this research are described and in Table 2.3 all of the variable names, types and their ranges can be shown.

Table 2.3 List of variables and domain values

Variable	Data type	Acceptable values
1. Gender	Boolean	Male = 0, female = 1
2. Education	Integer	1-5 = 1, 5-12 = 2, 12+ = 3
3. Age	Integer	65 and above
4. MMSE	Integer	Between 0 and 30, 25 and above means healthy brain activities

5. GDS	Integer	1 = normal, 2 = mild memory loss, 3 = MCI, 4 = early dementia, 5 = moderate dementia, 6 = moderately severe dementia, 7 = severe dementia
6. CDR	Decimal	0 = no cognitive impairment, 0.5 = questionable, 1 = mild dementia, 2 = moderate dementia, 3 = severe dementia
7. CDR – SB	Decimal	Between 0 and 18, reverse ratio between score and mental state
8. GerDS	Integer	1 to 10 is considered as "within normal range", 10 to 20 is considered as "mild depression", 20 to 30 is considered as "moderate to severe depression"
9. GerDS - 2nd Examine	Integer	1 to 10 is considered as "within normal range", 10 to 20 is considered as "mild depression", 20 to 30 is considered as "moderate to severe depression"
10. BOMC	Integer	Between 0 and 28, reverse ratio between score and mental state
11. BDRS	Decimal	Between 0 and 28, reverse ratio between score and mental state

2.2.1 MMSE

The Mental Status Examination is generally done to evaluate cognitive functioning of subjects and one of the well-known form is Mini-Mental State Examination (MMSE). It is developed by M. F. Folstein, S. E. Folstein and P. R. McHugh in 1975. In depth, it is used to detect and estimate the severity of the disease and predict the dementia (Folstein, Folstein and McHugh 1975). As a highly informative neuropsychological test, 10 – 25

percent of subjects whom score are considered in moderate range, may developed dementia in following 2 years (Kaufman 1991).

Researches show that (Fischer et. al. 2004) MMSE's criteria generally covers the following issues:

Appearance: gestures and mimics, patient's dress, attitudes and eye contact.

Orientation: Patient's focus, awareness to people and place.

Speech: Rate, tone, articulation, grammar.

Cognitive functioning: Vocabulary, reasoning, judgment, rational thoughts.

Emotional state: Mood and range of emotions.

Insight and judgment: Level of insight and comport themselves properly.

Attention, concentration and memory: recall of recent information.

As a clinical data, Turkish version (Gungen et. al. 1999) of Mini-Mental State Examination (MMSE) is used. Original Folstein's mini-mental state exam can be shown in below. The test that is used in this research can be found in Appendix 1.

1. Orientation

Each question is one point, correct answers graded as a one point.

1. What is today's date?

2. What is today's year?

3. What is the month?

4. What day is today?

5. Can you also tell me what season it is?

6. Can you also tell me the name of this hospital / clinic?

7. What floor are we on?

8. What city are we in?

9. What country are we in?

10. What state are we in?

2. Immediate Recall

First of all, the words *"ball", "flag", "tree"* are told by doctor slow and clearly. Then, the doctor is asked to the subject to repeat every word. If three of them is said correctly then the maximum score 3 is given.

3. Attention and Calculation

A. Counting Backwards Test

The subjects starts from 100 and count backwards by 7. Each response is recorded until 65. If all of them correct maximum score 5 is given. Any response that exactly less than 7 of previous record can accepted as a correct.

B. Spelling Backwards Test

Spell the word "world" backwards is asked to subject. Each letter is one point and if all of them true the maximum score 5 is given.

C. Final Score

Counting Backwards Test and Spelling Backwards Test's scores are compared and the greater one is written as a final score of Attention and Calculation part.

IV. Recall

The doctor is asked to the subject to recall the three words that is told in Immediate Recall part. One point is given for each correct response. So if the subject can remember the words *"ball", "flag", "tree"*; maximum score 3 is given.

V. Language

A. Naming

The doctor shows a wrist watch then asked to subject what it is. Same process is done for pencil. For each correct name of objects, 1 point is given and total score is 2.

B. Repetition

The doctor asked to subject to repeat: "No, ifs, ands, or, buts." One point is given for correct repetition.

C. Three Stage Command

First of all the subject's dominant hand is established. Then a sheet is given to subjects and three commands are given: "takes paper in hand", "folds paper in half", "puts paper

on floor.” For each correct response to commands one point is given. Maximum score is 3 if all of the responses are correct.

D. Reading

The doctor holds up the cards that written “Close your eyes” and asked to subject to read and do what it says. If the subject close his / her eyes one point is given.

E. Writing

A sheet is given to subjects and doctor asked to subject to write a sentence spontaneously. If the sentence has verb and subjects one point is given. Grammar and punctuation are not necessary.

F. Copying

Doctor shows intersecting pentagons, as shown in Figure 2.1 and ask him / her to draw it to sheet. If there are ten angles and two intersects one point is given. Tremor and rotation are ignored.

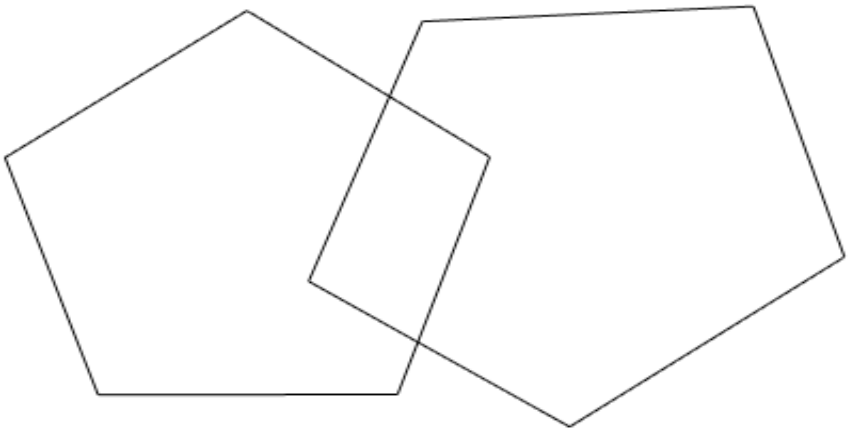


Figure 2.1: Intersecting pentagons

2.2.2 GDS

The Global Deterioration Scale (GDS) was developed by Barry Reisberg in 1982. The test divides the primary degenerative dementia to 7 different stages (Reisberg et. al. 1982).

The original GDS test can be shown in below. The test that is used in this research can be found in Appendix 2.

Stage 1 - No cognitive decline: There is no memory deficit during the clinical interview.

Stage 2 - Very mild cognitive decline: In this stage, memory deficit can be shown due to aging. Forgetting the place of familiar objects, forgetting well-known people's name are general signs of this stage.

Stage 3 - Mild Cognitive Decline: The stage of MCI. Some of the symptoms are: Patient may have lost when go to unfamiliar location, poor performance during the work, hard to remember new people name, concentration deficit, decreasing performance in social affairs.

Stage 4 – Moderate Cognitive Decline: The advanced form of MCI. Decreased information about the recent event, loss of personal history, Lack of ability about travel, handle finances, recognition familiar persons and inability to do complex tasks are main symptoms of this stage.

Stage 5 – Moderately Severe Cognitive Decline: In this stage, patients need some assistance do some activities but patients can do mandatory daily activities such as go to toilet or eating. Patients can't easily remember telephone numbers or address that patients know from a long time or have some difficulties to count back from 20 by 2s.

Stage 6 – Severe Cognitive Decline: In this stage, patients commonly retain well-known information such as their name, the year, the season but have difficulties to remember exact date or count back from 10. Obsessive and anxiety symptoms, agitation, emotional and mood changes occur. They need an assistance to daily activities and travel. On the other hand, they may go to familiar locations.

Stage 7 – Very Severe Cognitive Decline: In the last stage, patient will lost all of abilities to do daily activities. Verbal activities and basic psychomotor skills are completely lost. Patient need assistance to go to toilet, eating or go somewhere.

2.2.3 CDR and CDR – SB

The Clinical Dementia Rating (CDR) was developed in 1979 (Hughes et. al. 1982). CDR covers patient's six basic functions: memory, orientation, judgment, social affairs, hobbies and self-care.

CDR defines the level of impairment that range between 0 and 3. In other words range between "none" to "severe impairment". Respectively this score is, CDR = 0 means no dementia, CDR = 0.5 means questionable dementia, CDR = 1 means mild dementia, CDR = 2 means moderate dementia, CDR = 3 means severe dementia. Over the years, this categorization was expanded, so two more classify is used. These are CDR = 4 means questionable dementia and CDR = 5 means terminal (Dooneief et. al. 1996). As researches assert, CDR - SB is also used to evaluate of patient's mental stage in longitudinal studies (Cortes et. al. 2008) and there is high correlation between CDR - SB and dementia risks. In the study which set out to determine CDR and CDR - SB, CR - SB is more useful than CDR to analyze mild cognitive impairments (Lynch et. al. 2006). Sum of boxes of CDR (CDR - SB) defines the mental state using points between 0 and 18. Higher points indicates subject's severe and critical mental state.

The original CDR test can be shown in below (Morris, 1997). The test that is used in this research can be found in Appendix 3.

Healthy - CDR 0:

*Memory***:** No memory loss or slight inconsistent forgetfulness
*Orientation***:** Fully oriented

Judgment and Problem Solving: Solves everyday problems well; judgment good in relation to past performance
Community Affairs: Independent function at usual level in job, shopping, business and financial affairs, volunteer and social groups
Home and Hobbies: Life at home, hobbies, intellectual interest well maintained
Personal Care: Fully capable of self-care

Questionable dementia - CDR 0.5:

Memory: Mild consistent forgetfulness: partial recollection of events: "benign" forgetfulness
Orientation: Fully oriented
Judgment and Problem Solving: Only doubtful impairment in solving problems, similarities, differences
Community Affairs: Only doubtful mild impairment in these activities
Home and Hobbies: Life at home, hobbies, intellectual interest well maintained
Personal Care: Fully capable of self-care

Mild dementia - CDR 1:

Memory: Moderate memory loss, more marked for recent events; defect interferes with everyday activities
Orientation: Some difficulty with time relationship; oriented for place and person at examination but may have geographic disorientation
Judgment and Problem Solving: Moderate difficulty in handling complex problems; social judgment usually maintained
Community Affairs: Unable to function independently at these activities thought may still be engaged in some; may still appear normal to casual inspection
Home and Hobbies: Mild but definite impairment of function at home; more difficult chores abandoned; more complicated hobbies and interests abandoned
Personal Care: Need occasional prompting

Moderate dementia - CDR 2:

Memory: Severe memory loss; only high learned material retained; new material rapidly lost
Orientation: Usually disoriented
Judgment and Problem Solving: Severely impaired in handling problems… similarities; differences: social judgment usually impaired
Community Affairs: No pretense of independent function outside the home. Appears well enough to be taken to functions outside a family home
Home and Hobbies: Only simple chores preserved, very restricted interests, poorly sustained
Personal Care: Requires assistance in dressing, hygiene, keeping of personal effects

Severe dementia - CDR 3:

Memory: Severe memory loss; only fragments remain
Orientation: Orientation to person only
Judgment and Problem Solving: Unable to make judgments or solve problems
Community Affairs: No pretense of independent function outside the home. Appears too ill to be taken to functions outside a family home
Home and Hobbies: No significant function in home or outside of own home
Personal Care: Requires much help with personal care; often incontinent

2.2.4 GerDS

The Geriatric Depression Scale (GerDS) is measure depressive symptoms using 30 yes - no questions. It was developed in beginning of 80's (Brink et. al. 1983). At that time, it was common to misdiagnose nondepressed elderly people as a depressed patients due to the somatic symptoms. It was developed to minimize to the misdiagnosis.
In GerDS, each question has one point and summation range vary between 0 and 30. As an inverse ratio, when the results getting closer to 30 points, possibility of disorder brain

activities getting higher. Generally it takes 5 to 10 minutes to complete. Even though GerDS developers scores 10 or less categorized as “within the normal range” scores between 11 and 20 categorized as “mild depression” and between 21 and 30 categorized as “moderate to severe depression”, researches show that (Strauss et. al. 2006) while a cutoff score > 9 may suitable to define healthy society, cutoff score > 12 may suitable the classify “medical inpatients”. In this thesis, the most common one, original categorization is used. GerDS - 2nd Examine score is given when subject’s next visits after first interview. The original GerDS test can be shown in below. The test that is used in this research can be found in Appendix 4.

1. Are you basically satisfied with your life?
2. Have you dropped many of your activities and interests?
3 .Do you feel that your life is empty?
4. Do you often get bored?
5. Are you hopeful about the future?
6. Are you bothered by thoughts you can't get out of your head?
7. Are you in good spirits most of the time?
8. Are you afraid that something bad is going to happen to you?
9. Do you feel happy most of the time?
10. Do you often feel helpless?
11. Do you often get restless and fidgety?
12. Do you prefer to stay at home, rather than going out and doing new things?
13 .Do you frequently worry about the future?
14. Do you feel you have more problems with memory than most?
15. Do you think it is wonderful to be alive now?
16. Do you often feel downhearted and blue?
17. Do you feel pretty worthless the way you are now?
18. Do you worry a lot about the past?
19. Do you find life very exciting?
20. Is it hard for you to get started on new projects?
21. Do you feel full of energy?
22. Do you feel that your situation is hopeless?

23. Do you think that most people are better off than you are?

24. Do you frequently get upset over little things?

25. Do you frequently feel like crying?

26. Do you have trouble concentrating?

27. Do you enjoy getting up in the morning?

28. Do you prefer to avoid social gatherings?

29. Is it easy for you to make decisions?

30. Is your mind as clear as it used to be?

2.2.5 BOMC

The Blessed Orientation – Memory – Concentration (BOMC) was developed by Katzman. Actually BOMC is shortened form of Blessed Information-Memory-Concentration (BIMC) test. Katzman and colleagues analyzed and selected 6 out of 29 items from BIMC for to correlate between neuropathologic and cognitive alterations, graduation of cognitive and functional scale in dementia (Katzman et. al. 1983).
In this test, questions are order from easy to difficult and usually takes less than 5 minutes.

The original BOMC test can be shown in below. The test that is used in this research can be found in Appendix 5.

1. What year is it now?

2. What month is it now?

Memory phase - Repeat it:

"John Brown, 42 Market Street, Chicago."

3. About what time is it? (Within 1 hour)

4. Count backwards 20 to 1.

5. Say the months in reverse order.

6. Repeat the memory phrase: "John", "Brown", "42", "Market", "Chicago"

If the subject cannot recall the year, 1 point is given and multiplied by 4. Second and third questions are graded as 1 and multiplied by 3 if the subject cannot remember the month, phrases and time. In question 4 and 5, for uncorrected errors score 2, for self-corrected errors score 1 and for no errors score 0 is given and these points are multiplied by 2. In the last question, for each uncorrected words 1 point is given and multiplied by 2.

2.2.6 BDRS

The Blessed Dementia Rating Scale (BDRS) was developed in 1968. Blessed and his friends tried to evaluate elderly people's "degree of intellectual and personality deterioration" (Blessed, Tomlinson and Ruth 1968). The rating scale has 22 items and is divided into 3 parts. First 8 items checks daily activities such financial issues or find an address. If the patient is able to perform the item, score of 0 is given.

BDRS is scored out of 28 points and higher points mean larger deterioration about brain functions. Score of ½ is given for partial performance and score of 1 is given. Next part is about habits and self-care and includes 3 questions. In this section scores are given between 0 and 3 with the same mentality of previous one. The last part checks one's personality and interest with 11 questions. If any changes in personality or interests, items are scored 1 or 0 if there is no changes. As a criteria, 4 points and below indicates there is no cognitive disorder, scores between 4 and 9 point that MCI and 10 or higher scores are limits from moderate to severe impairment. (Eastwood et. al. 1983) In addition, researches affirmed that 15 is threshold for moderate impairment (Stern et. al. 1987).

The original BDRS test can be shown in below. The test that is used in this research can be found in Appendix 6.

Changes in performance of everyday activities

1. Inability to perform household tasks

2. Inability to cope with small sums of money

3. Inability to remember shortlist of items; for example, in shopping list

4. Inability to find way about indoors

5. Inability to find way about familiar streets

6. Inability to interpret surroundings; for example, to recognize whether in hospital or at home; to discriminate between patients, doctors, nurse, relatives, other hospital staff, etc.

7. Inability to recall recent events; for example, recent outings, visits of relatives or friends to hospital, etc.

8. Tendency to dwell in the past

Changes in habits

9. Eating

(0) = cleanly, with proper utensils

(1) = messily, with spoon only

(2) = simple solids (for example, biscuits)

(3) = has to be fed

10. Dressing

(0) = unaided

(1) = occasionally misplaced buttons, etc.

(2) = wrong sequence, commonly forgetting items

(3) = unable to dress

11. Sphincter control

(0) = complete control

(1) = occasional wet bed

(2) = frequent wet bed

(3) = doubly incontinent

Changes in personality, interests, drive

12. Increased rigidity

13. Increased egocentricity

14. Impairment of regard of feeling for others

15. Coarsening of affect

16. Impairment of emotional control (for example, increased petulance and irritability)

17. Hilarity in inappropriate situations

18. Diminished emotional responsiveness

19. Sexual misdemeanor (arising de novo in old age)

20. Hobbies relinquished

21. Diminished initiative or growing apathy

22. Purposeless hyperactivity

2.3 FEATURE SELECTION FOR DATA MINING SOLUTION

Machine can learn problem from data set or database according to attributes' prior information. To rank information, information gain method is used to approximate quality of attributes via entropy. This method estimates the difference between prior and post entropy (Kononenko, 1994).

Assume that *C* and *V* are discrete variables and *C*'s prior entropy is symbolized as *E (C)*

E (C) = $-\sum_c P(C)\, log_2\, P\ (C)$ where *P (C)* is the probability function of *C*.

As a post entropy of *C* given *V*

E (C\V) = $\sum_v P\ (V)\ E(C \setminus V)$

= $-\sum_V P\ (V) \sum_C P\ (C \setminus V)\, log_2\, P\ (C \setminus V)$

The information gain *IG(C; V)* is

IG (C; V) = E (C) – E (C\V)

IG (C; V) = $-\sum_c P(C)\, log_2\, P\ (C) - \sum_v(-P\ (V)\ \times \sum_C P\ (C \setminus V)\, log_2\, P\ (C \setminus V)$

Before applying algorithms, attribute ranking function is applied using information gain ranking filter in Waikato Environment for Knowledge Analysis (WEKA) platform which is a machine learning software written by Java and measures information gain of variables. During this process, numeric attributes are firstly discretized by using MDL-based discretization method (Witten and Frank, 2005). According to this model, the most significant parameters that affect the fuzzy model are chosen. Table 2.4 shows the variables in descending ratio. According to the rankings, gender and age which are ranked less than 5 percent are eliminated.

In here, the important things is all of the patient's ages are 65 or older, so this elimination says that age and gender does not make a difference if the age segment is selected 65 or over. Even though women have mildly elevated risk than men, in this research the data set is chosen from the late-onset subjects. As has been noted that, the mean age of the data set is 76.85 ± (6.25). The conducted research about the age is stressed that (Farrer et. al. 1997) AD and age correlation is fairly enough between 40 and 90, but the effect of age is decreasing after age 70. In addition, another research that examines the relation between gender and dementia, (Ruitenberg et. al. 2001) declared that there is no significant gender difference up to age 90. In this data set, for women mean age is 76.56 ± (6.57) and for men' is 77.12 ± (5.96); so our findings is rational with the previous research.

Table 2.4: Variables and rank percentages

Rank Percentage	Variable
0.76362	CDR
0.76363	GDS
0.6335	CDR - SB
0.60051	BDRS
0.34984	BOMC
0.14297	MMSE
0.10903	GerDS
0.09358	Education
0.0029	Gender
0.00048	Age

2.4 PREDICTING AD BY ANFIS

As a neural-fuzzy system, ANFIS is fusion both fuzzy systems and neural networks. It was introduced by Jang. This non-linear mapping system uses fuzzy logic and learning logic of artificial neural networks with capability of automated adaption about to training sets and interpretability. The system is operated by nodes, directional links and outputs are calculated by last rightmost node in networks (Jang 1993).

There are two main goals for Neuro-fuzzy systems. First one is high accuracy for prediction, classification or approximation of the problem using training sets and the second one is, instead of neural network's black boxes, neural fuzzy systems creating rules with transparency and prior knowledge.

In fuzzy reasoning, the compositional rule can be described with modus ponens tautology. In this example *x, y* are variables *and A, B, A′, B′* are fuzzy sets.

Premise: x is A′
Implication: IF x is A THEN y is B
Conclusion: y is B′

In Sugeno-type fuzzy inference system, if-then rules are used (Sugeno and Kang 1988; Takagi and Sugeno 1985). These two rules can be expressed as,

Rule 1: If X is A1 and Y is B1, then f1 = p1x + q1y + r1
Rule 2: If X is A2 and Y is B2, then f2 = p2x + q2y + r1

Fuzzy Inference systems can be described as a nonlinear mapping process. In this process, inputs are converted from numerical domain to fuzzy domain. For this procedure, fuzzy sets and fuzzifiers are used. Then fuzzy rules and fuzzy inference engine are utilized. In fuzzy inference system, the data that comes from the fuzzifiers generates into the rules and in the last process is transformed the fuzzy domain to numerical domain back using defuzzifiers. This process can be shown in Figure 2.2:

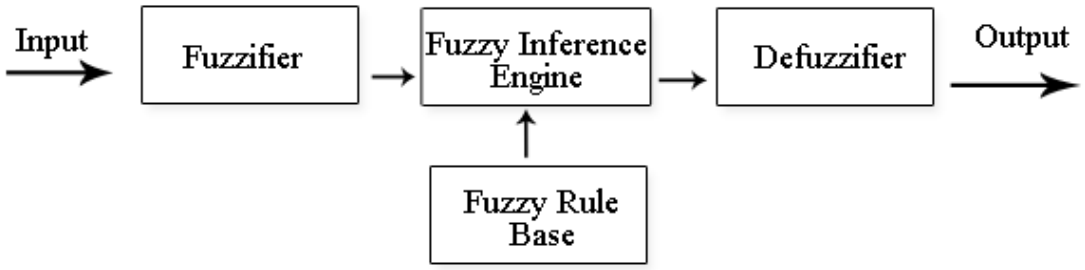


Figure 2.2: Fuzzy Inference System Work Scheme

As it mentioned above, the structure of ANFIS which combines ANN and fuzzy system, make a hybrid structure and using the two popular learning algorithm: least square estimation method and back-propagation gradient descent algorithm. This hybrid system prevents itself from over-fit or not-fit data with the highly convenient attributes: number of training epochs, fuzzy rules and membership functions. Hybrid learning sets in from two items: forward pass and backward pass. Until to Layer 4, the forward pass signals get through the layers and in Layer 4 connected parameters are identified via Least Square Method and in backward pass, the errors are back propagated until the lowest error are found. Figure 2.3 shows the brief summary of two-input first-order Sugeno fuzzy model with two rules.

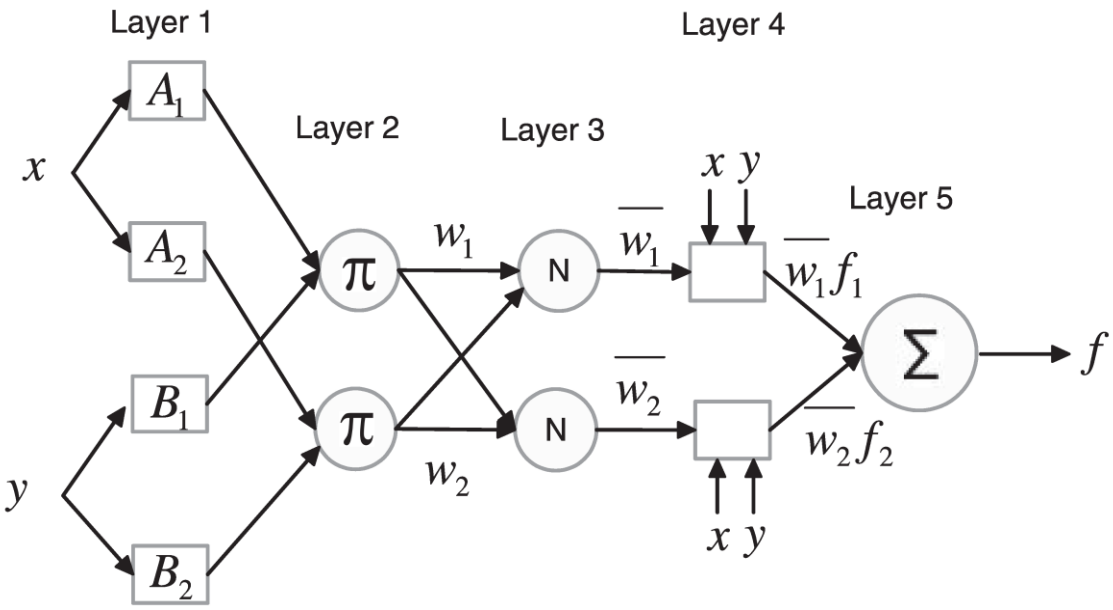


Figure 2.3: Summary of two-input first-order Sugeno fuzzy model

Layer 1: First layer, also known as fuzzy layer, nodes can be described as A1, A2, B1, B2 which are the linguistic labels (small, large, etc.), and they are used in the system to separate the membership functions. For instance, the node function in this layer can be expressed the generalized membership function between input and output:

$$\mu A_i(x),\ i = 1,2. \qquad \textbf{(2.1)}$$

$$\mu B_i(x),\ j = 1,2. \qquad \textbf{(2.2)}$$

Layer 2: In this layer, T-norm operator performs the firing strength that represented by w_i for each node. The output w1 and w2 functions computes the incoming signals,

$$\mathcal{W}_i = \mu A_i(x)\ \mu B_i(y),\ i = 1,2. \qquad \textbf{(2.3)}$$

Layer 3: Fixed nodes normalize the firing strength and calculates the ratio for that node to the sum of all rules fires strength.

$$\bar{w}_i = \frac{w_i}{w_1 + w_2},\ i = 1,2. \quad \textbf{(2.4)}$$

Layer 4: The layer's nodes are adaptive and linked with the previous layer where the layer takes the linear and consequent parameter.

$$\bar{w}_i f_i = \bar{w}_i (p_i x + q_i y + r_i),\ i = 1,2. \quad \textbf{(2.5)}$$

Layer 5: The last one also known as aggregation layer calculates the overall output as total of incoming signals of the system.

$$\sum_i \bar{w}_i f_i = \frac{\sum_i w_i f_i}{\sum_i w_i} \quad \textbf{(2.6)}$$

ANFIS's learning rule which is back propagation gradient descent calculates the all of the nodes outputs' derivative of squared error. This method is done by the ANFIS.

2.5 PREDICTING AD BY MLPS

Multilayer Perceptron (MLP) algorithm uses feed-forward architecture and generally is preferred for supervised learning task. This algorithm sets connection weights using iterative training methods with at least three layers. A typical multilayer perceptron network's first layer referred as an input layer; then, one or more hidden layers and lastly output layer. Basic structure of multilayer perceptron can be shown in Figure 2.4:

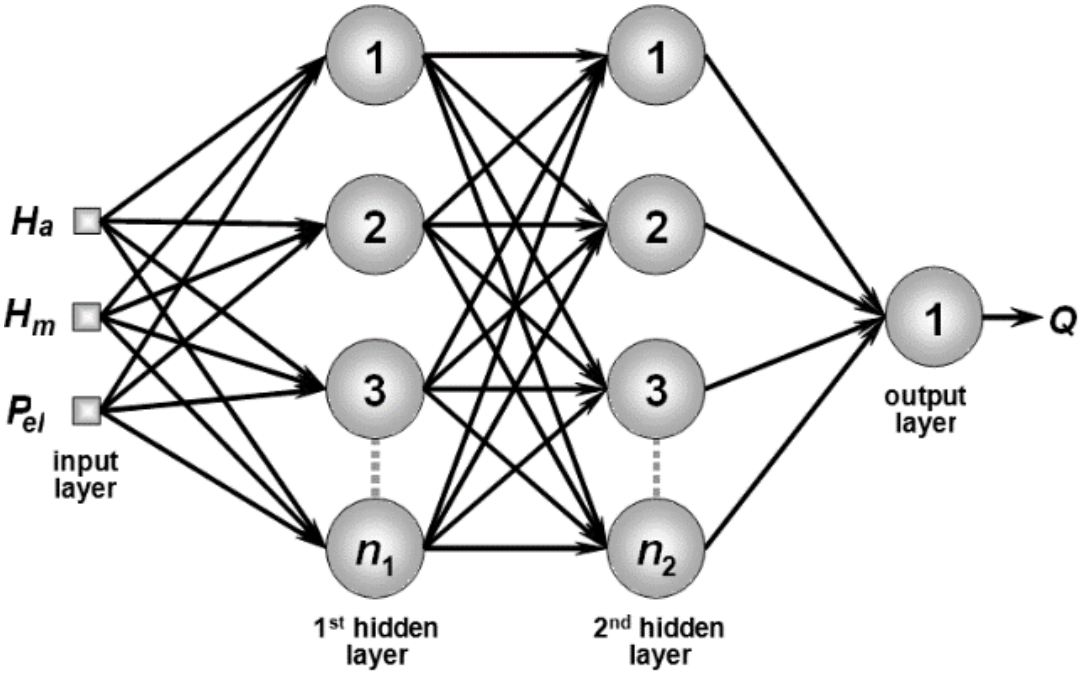


Figure 2.4: A schematic diagram of multilayer perceptron algorithm

In this algorithm, inputs are associated with weights and outputs have an activation function. Using nonlinear activation function for each neuron makes difference of other perceptron algorithms. As a supervised learning technique, it occurs via changing connection weights between each neuron and comparing the error and output results. For further details and explanation about the multilayer perceptron can be found in various articles (Ruck, Roger and Kabrisky 1989; Ruck et. al. 1990; Pal and Mitra 1992).

2.6 PREDICTING AD BY ID3

Iterative Dichotomiser 3 (ID3) is a decision tree algorithm (Quinlan 1986). In this nonincremental algorithm decision sequence is selected based on information gain using entropy. Entropy is used to determine how informative a node is. It is calculated using the formula:

$$E(S) = \sum_{j=1}^{n} fs(j)\, log_2\, f_s(j) \qquad \textbf{(2.7)}$$

where

$E(S)$ is the information entropy of the set *S*;
n is number of *S*'s different values
$fs(j)$ is the frequency of the value j in the set *S*
log_2 is the binary algorithm.
If the entropy is 0 then classified set is identified perfectly.

After the entropy, Information Gain uses to decide which attribute is the most suitable for improved entropy. The column that has the highest information gain as used as a node of decision tree. Information Gain is calculated using the formula:

$$Gain(S, A) = Entropy(S) - \sum_{i=1}^{m} f_s(A_i) E(S_{A_i}) \quad \textbf{(2.8)}$$

where
G(S, A) is the information gain of the set *S* after splitting over *A*
Entropy(S) is the information entropy of the set *S*
M is the number of the different values of the attribute *A* in *S*
$f_s(A_i)$ is the frequency of A_i items as value *A* in *S*
A_i is the i^{th} possible value of *A*
S_{A_i} is a subset of *S* an it contains all *i*.

Unlike a binary tree, the ID3 decision tree can have multiple children and siblings. This algorithm searches through the training set's attributes and choose the best one. The algorithm works recursively until the best attribute perfectly classifies the training set. The top-most node represents the highest information gain. The highest information gain means the most useful for classification. After the best attribute is selected, ID3 algorithm does not consider the previous choices to compare which one is more useful for classification. Results are used to classify future samples.

The pseudo code of ID3 algorithm is written below:

ID3 (Examples, Target_Attribute, Attributes)

Create a root node for the tree

If all examples are positive, Return the single-node tree Root, with label = +.

If all examples are negative, Return the single-node tree Root, with label = -.

If number of predicting attributes is empty, then return the single node tree Root, with label = most common value of the target attribute in the examples.

Otherwise Begin

A ← The Attribute that best classifies examples.

Decision Tree attribute for Root = A.

For each possible value, V_i, of A,

Add a new tree branch below Root, corresponding to the test A = V_i.

Let Examples(V_i) be the subset of examples that have the value V_i for A

If Examples(V_i) is empty

Then below this new branch add a leaf node with label = most common target value in the examples

Else below this new branch add the sub tree ID3 (Examples (V_i), Target_Attribute, Attributes – {A})

End

Return Root

2.7 PREDICTING AD BY ONER

One Rule (OneR) algorithm generates a one-level decision tree. The algorithm takes the single attribute that is the most accurate in predicting. It checks the training data and create one rule for every value of the chosen attribute. This process repeat itself for each attribute then number of errors are calculated to find each of attribute's total error. In the end, all of the attributes are analyzed according to error rate and smallest one chosen and determined as a "one rule". Researches (Holte 1993) show that this algorithm can give acceptable accuracy rate when the results are compared to more complex algorithms. OneR algorithm's pseudo code is written in below:

OneR Algorithm

For each predictor,

For each value of that predictor, make a rule as follows;

Count how often each value of target (class) appears

Find the most frequent class

Make the rule assign that class to this value of the predictor

Calculate the total error of the rules of each predictor

Choose the predictor with the smallest total error.

2.8 ANALYSIS METHODS

For comprehensive analysis, sensitivity, specificity, correctness and Root Mean Squared Error (RMSE) results are calculated using confusion matrix. Matrix values have the following definition:

TP (true positive): Number of records that prognosis of a patient's complaint is AD and the algorithm classified as an AD.

TN (true negative): Number of records that prognosis of a patient's complaint is AD and the algorithm classified as a not AD.

FP (false positive): Number of records that prognosis of a patient's complaint is not AD and the algorithm classified as AD.

FN (false negative): Number of records that prognosis of a patient's complaint is not AD and the algorithm classified as not AD.

And the results are computed according to the following formulas:

$$Sensitivity\ (\%) = \frac{TP}{TP+FN} \times 100 \quad \textbf{(2.9)}$$

$$Specificity\ (\%) = \frac{TN}{TN+FP} \times 100 \quad \textbf{(2.10)}$$

$$Correctness\ (\%) = \frac{TP+TN}{TP+FP+FN+TN} \times 100 \quad \textbf{(2.11)}$$

$$Root\ Mean\ Squared\ Error\ (\text{RMSE})\ (\%) = \sqrt{\frac{\sum_{i=1}^{N}(pi-ri)^2}{N}} \quad \textbf{(2.12)}$$

where p_i is the predicted values, r_i is the real values and N is the number of records.

For ANFIS, MATLAB codes are used and can be shown in below.

RMSE.m

```
% Load files
load c:\thesis\trainingSetInput.txt
load c:\thesis\trainingSetOutput.txt
load c:\thesis\trainingSet.txt
load c:\thesis\controlSet.txt
load c:\thesis\controlSetInput.txt
load c:\thesis\controlSetOutput.txt
load c:\thesis\testingSet.txt
load c:\thesis\testingSetInput.txt
load c:\thesis\testingSetOutput.txt
% Generate  fuzzy inference system
fismat = genfis2(trainingSetInput, trainingSetOutput, 0.5);
 % 3 epoches
for ct=1:3,
   [fismat,error] = anfis(trainingSet, fismat,2, NaN, controlSet, 1);
end;
% Evaluate of fuzzy inference system
predictedTrainingSetOutput = evalfis(trainingSetInput, fismat);
predictedTestSetOutput = evalfis(testingSetInput, fismat);
```

```
predictedControlSetOutput = evalfis(controlSetInput, fismat);
% RMSE calculation
numberOfRecords = 67;
difference = normalize(predictedTestSetOutput) - testingSetOutput;
RMSE = power(sum(power(difference,2)) / numberOfRecords, 1 / 2);
disp(RMSE);
```

normalize.m

```
function n = normalize(x)
%-------------------------------------------------------------
% This function normalizes the predicted output of a FIS as 4
% different clusters where parameter x is the output vector.
%-------------------------------------------------------------
% assumed_prediction_classes = [1, 0.423, 0.1263, 0.8895, 0, 0.184, 0.9952];
n = x;
mid1 = ( 0.1 – 0 ) / 2;
mid2 = ( ( 0.3 - 0.1 ) / 2 ) + 0.1;
mid3 = ( ( 0.7 - 0.3 ) / 2 ) + 0.3;
mid4 = ( ( 0.9 - 0.7 ) / 2 ) + 0.7;
% scalings = [0, mid1, 0.1, mid2, 0.3, mid3, 0.7, mid4, 0.9];
% disp(scalings);
% disp(assumed_prediction_classes );
for i = 1 : length(n)
   if (n(i) <= mid1)
      n(i) = 0.1;
   elseif ( n(i) > mid1 && n(i) < 0.1 )
      n(i) = 0.1;
   elseif ( n(i) <= mid2 && n(i) > 0.1 )
      n(i) = 0.1;
   elseif ( n(i) > mid2 && n(i) < 0.3 )
      n(i) = 0.3;
   elseif ( n(i) <= mid3 && n(i) > 0.3 )
```

```
        n(i) = 0.3;
    elseif ( n(i) > mid3 && n(i) < 0.7 )
        n(i) = 0.7;
    elseif ( n(i) <= mid4 && n(i) > 0.7 )
        n(i) = 0.7;
    else
        n(i) = 0.9;
    end
end
% disp(assumed_prediction_classes );
```

3. FINDINGS

This study is divided into three parts to make a classification model. First phase's aim is collect and prepare the data; then the row data are filtered and functional attributes are selected using WEKA's information gain filter. In the last phase, methods are generated. Comprehensive analysis, sensitivity, specificity, correctness and RMSE values are given in Table 5. The outputs of these rules indicates four distinct classes. These classes are 0.1, 0.5, 0.7 and 0.9 show the state of patient's respectively Normal, MCI, PRAD and PosAD.

As mentioned in introduction, this research's proposed approach is to combine ANFIS and information gain method to predict AD and its phases. First of all, row data is filtered WEKA's *InfoGainAttributeEval* class to evaluate worth of the attributes according to their information gain rank. As a result of the filtering age and gender attributes are ruled out from the data set. For ANFIS, MATLAB's Fuzzy Logic Toolbox is used to generate fuzzy rules and advantages of using neural network structure of this fuzzy inference system. Then selected features are applied to ANFIS to both train and test data. Total 264 records are divided into two parts: training and test data. Training data has 197 (approximately 66 %) and test data has 67 records (approximately 33 %).

To construct the fuzzy inference system (FIS), in ANFIS, Sugeno-type fuzzy model and sub-clustering methods are used with the parameters of range of influence is 0.5, squash factor is 1.25, accept ratio is 0.5 and rejection ratio 0.15. As seen in Figure 3.1, ANFIS generated 5 rules and all of them help to make a connection between inputs and output. In other words, these rules lent assistance to gain insight to predict AD's in early phases.

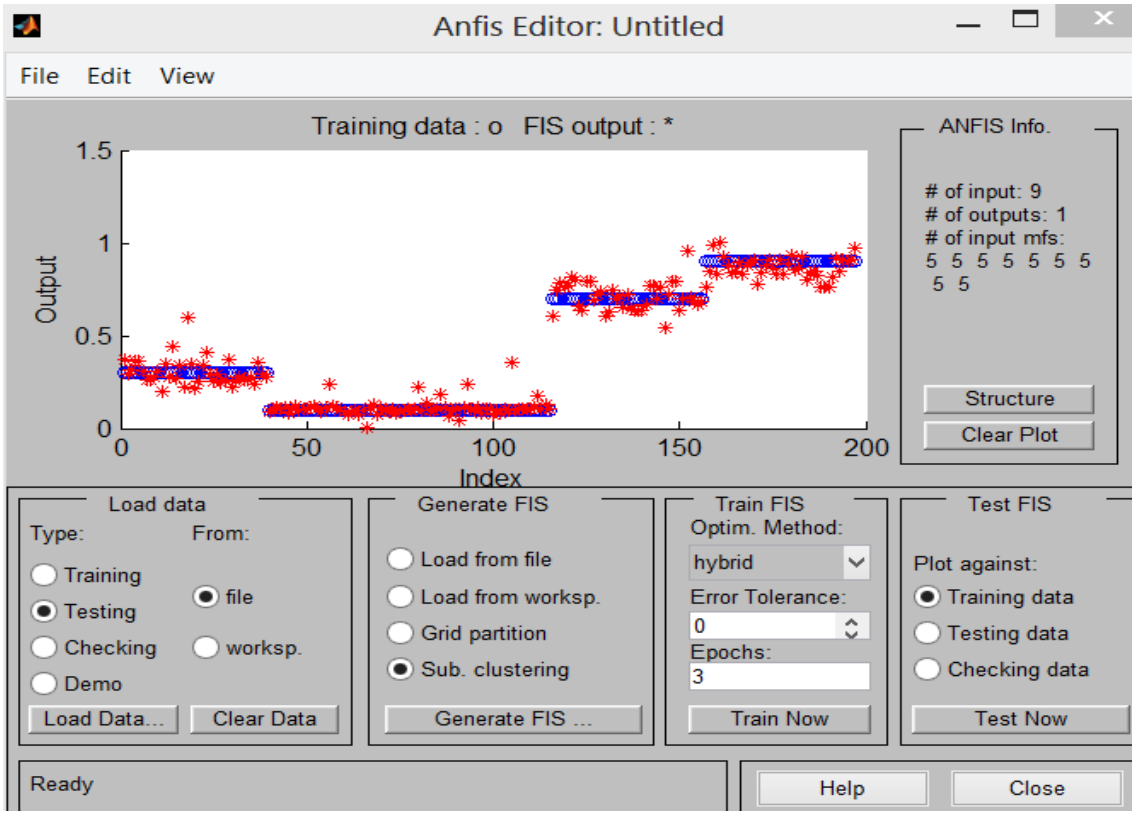


Figure 3.1: User interface of MATLAB's Fuzzy Logic Toolbox with 5 generated rules

5 rules that are developed by Fuzzy Logic Toolbox are written and described below.

Rule 1: [2 23 2 0 0 9 9 9 0] [0.1]

If Education Level = 2 and MMSE = 23 and GDS = 2 and CDR = 0 and CDR - SB = 0 and GerDS = 9 and GerDS 2nd Examine = 9 and BOMC = 9 and BDRS = 0 then Output is 0.1 which means Normal.

According to the rule this patient belongs to cluster 0.1 and determined as a Normal stated patient. The examine results show that, especially CDR, CDR - SB and BDRS results which are zero, make strength the idea about the patience's state.

Rule 2: [2 29 1 0 2 5 5 2 1] [0.1]

If Education Level = 2 and MMSE = 29 and GDS = 1 and CDR = 0 and CDR - SB = 2 and GerDS = 5 and GerDS 2nd Examine = 5 and BOMC = 2 and BDRS = 1 then Output is 0.1 which means Normal.

Similar to Rule 1, the Output is Normal. In this rule, particularly Mini-Mental Score is considerably enough to make the decision as a Normal state. In addition GDS and CDR scores support the thesis.

Rule 3: [3 22 4 1 7 13 12 14 4] [0,7]

If Education Level = 3 and MMSE = 22 and GDS = 4 and CDR = 1 and CDR - SB = 7 and GerDS = 13 and GerDS 2nd Examine = 12 and BOMC = 14 and BDRS = 4 then Output is 0.7 which means PosAD.

Even though Mini-Mental score is barely enough to say MCI state, rest of the parameters specifically both GerDS scores and BOMC value clearly stressed that patient state determined as a Possible Alzheimer.

Rule 4: [3 22 4 1 5 15 14 13 3] [0.7]

If Education Level = 3 and MMSE = 22 and GDS = 4 and CDR = 1 and CDR – SB = 5 and GerDS = 15 and GerDS 2nd Examine = 14 and BOMC = 13 and BDRS = 3 then Output is 0.7 which means PosAD.

Almost similar to previous rule; the parameters, except MMSE, support the idea of patient’s Possible Alzheimer state. . So this rule is also support the thesis lack of efficiency of gender about the AD.

Rule 5: [3 12 6 3 16 16 16 14 4] [0,9]

If Education Level = 3 and MMSE = 12 and GDS = 6 and CDR = 3 and CDR - SB = 16 and GerDS = 16 and GerDS 2nd Examine = 16 and BOMC = 14 and BDRS = 4 then Output is 0.9 which means PRAD.

The last rule's output clearly shows that the patient's state. MMSE score is considerably below the average and both CDR and GerDS scores reached the top limit. Moreover, BOMC and BDRS scores highly stressed the patient's state which is Probably Alzheimer. All of the rules and their results show that ANFIS has considerably high prediction rate with the 97 percent. The correlation between the rules are shown in Figure 32:

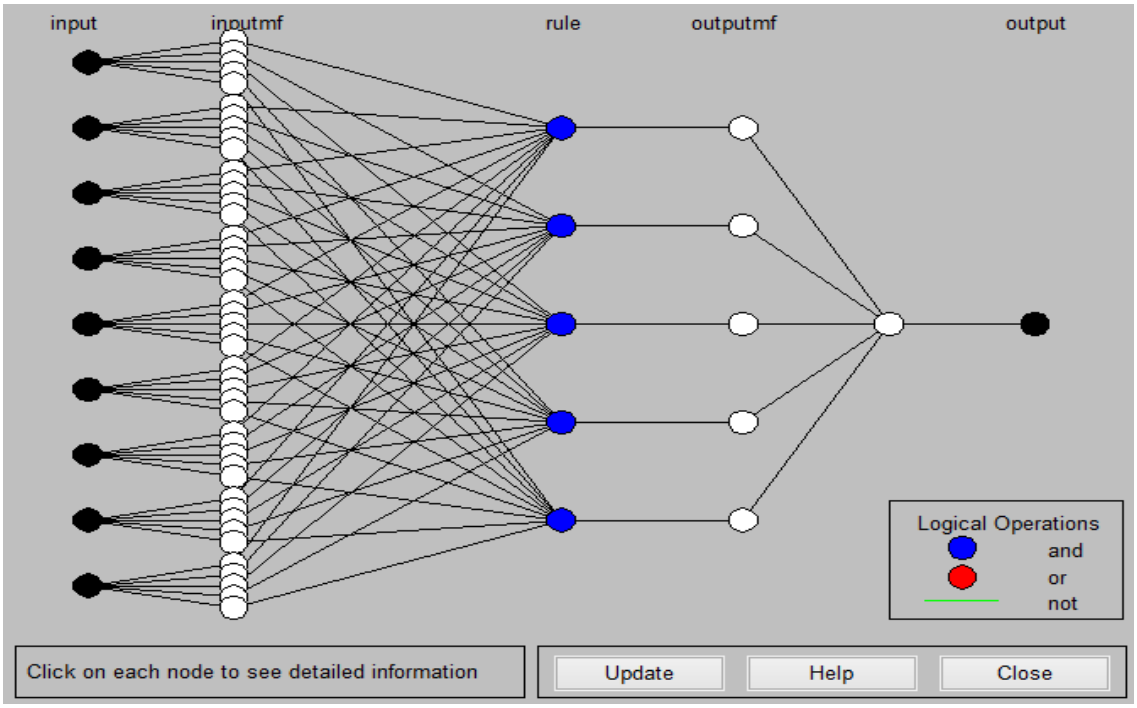


Figure 3.2: Relations between inputs, rules and output.

After the ANFIS MLP, ID3 and OneR algorithms, WEKA 3.7 tool is used and built classification model. The data is revised to create WEKA data files ".arff". As it mentioned before, attribute selection is used to find a minimal set of attributes.
For the other three algorithms, except gender and age, the all other attributes that preserve the class distribution.

As seen in Figure 3.3, MLP has a 87 percent prediction rate the algorithm can make a correct classification. MLP's specificity rate is 87 percent, correctness rate is 87 percent and RMSE rate is 23 percent.

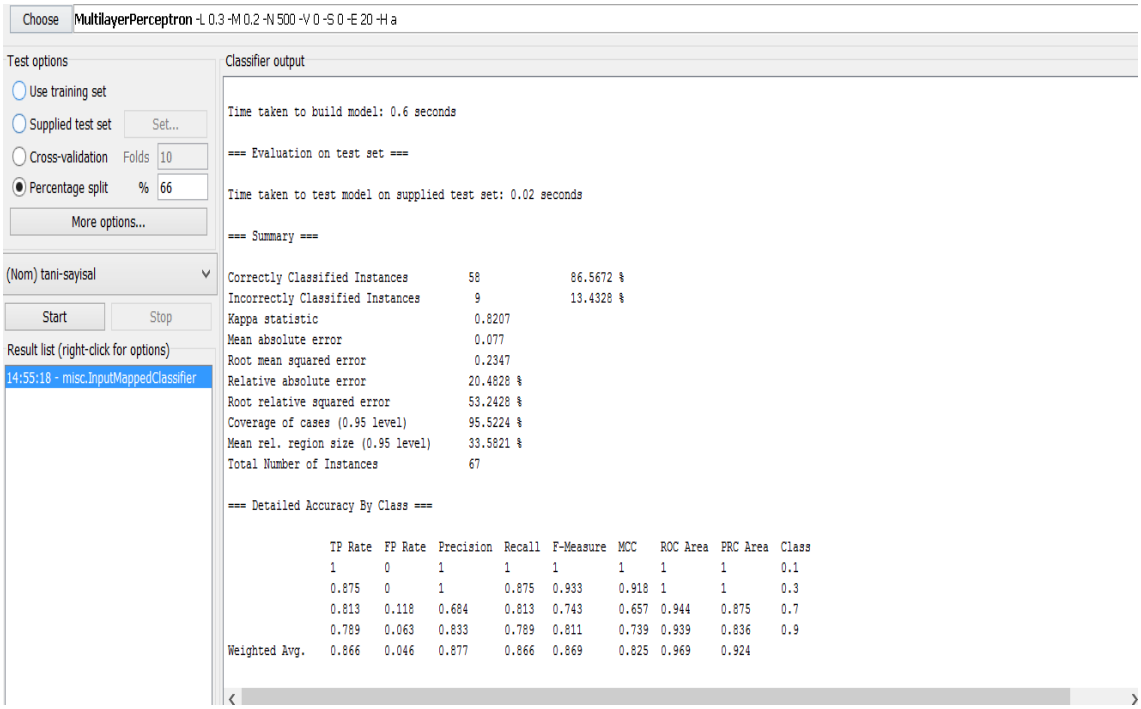


Figure 3.3: Multilayer perceptron's output summary and accuracy results

As seen in Figure 3.4, OneR has a 76 percent prediction rate the algorithm can make a correct classification. OneR's specificity rate is 69 percent, correctness rate is 87 percent and RMSE rate is 23 percent.

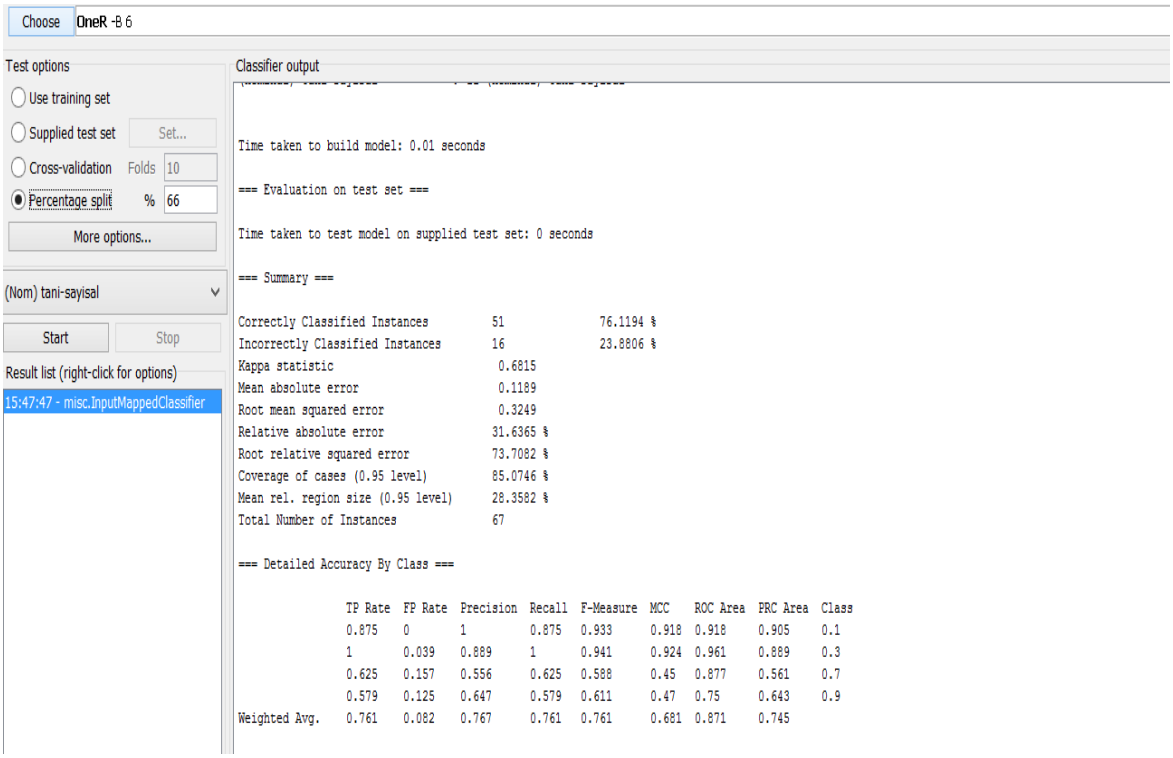


Figure 3.4: OneR's output summary and accuracy results

As seen in Figure 3.5, ID3 has an 87 percent prediction rate the algorithm can make a correct classification. ID3's specificity rate is 70 percent, correctness rate is 70 percent and RMSE rate is 76 percent.

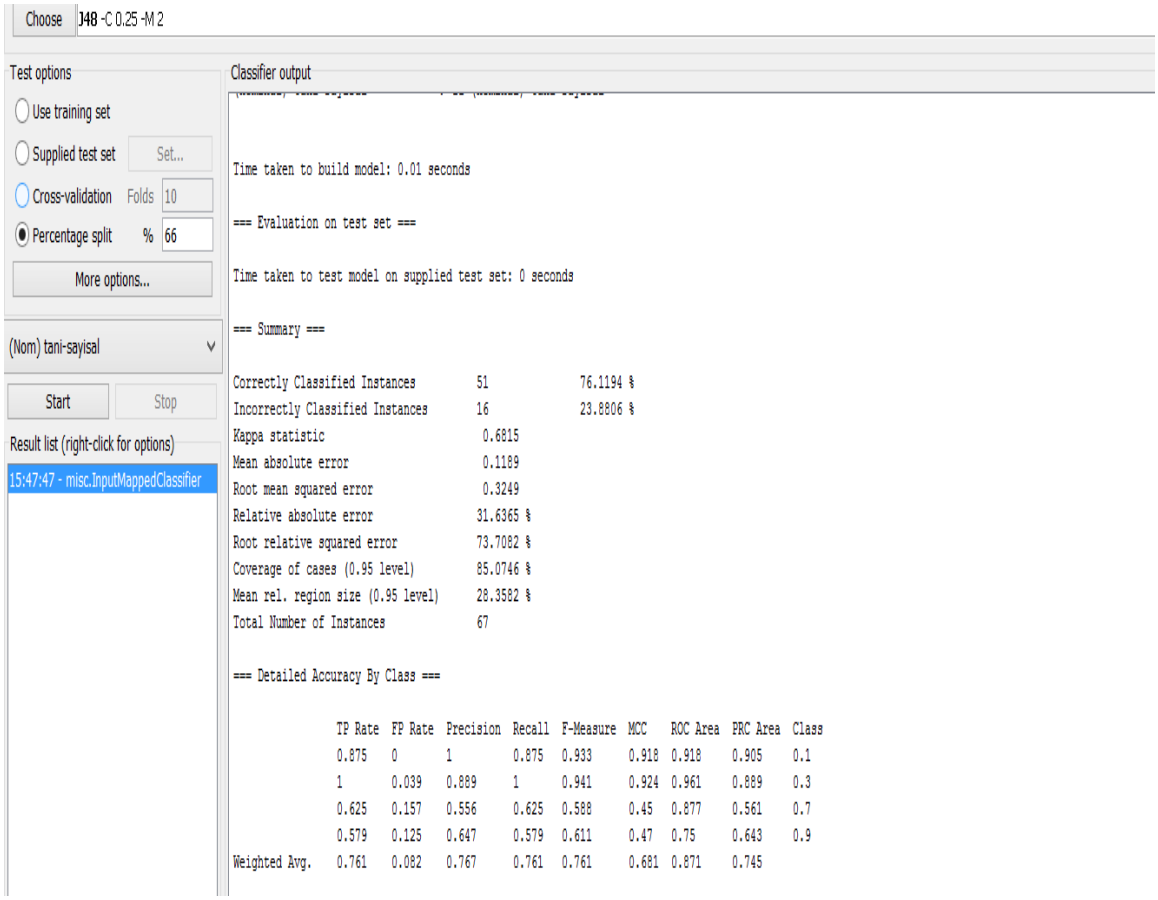


Figure 3.5: ID3's output summary and accuracy results

As shown in Table 3.1, the other two algorithm ID3 and OneR have prediction rates much less than ANFIS. With 96 percent correctness rate ANFIS has a highly accurate to predict AD and its phases. Table X shows the prediction rate comparison between the algorithms.

Table 3.1: Prediction rate comparison of the algorithms

Method name	Sensitivity	Specificity	Correctness	RMSE
ANFIS	0.97	0.96	0.96	0.06
MLP	0.82	0.82	0.87	0.23
OneR	0.69	0.69	0.76	0.32
ID3	0.70	0.70	0.76	0.33

4. CONCLUSION

In this study 264 different number of subjects' record are analyzed according to 11 attributes. Filtering results show that, gender and age's effects are not enough to take into consideration for AD in late – onset subjects. According to the results of the study, ANFIS is more accurate and reliable way to make a classification. Benchmarking results also support that ANFIS model developed classifies of subjects with a highly reasonable rates. In addition, all of the comparison criteria which are sensitivity, specificity, correctness, RMSE have higher acceptable rates when the comparison with the other algorithms. As a further studies and better results, number of subjects' records will be augmented, so algorithms can acquire different experiences from variety of subjects. By the same token, increment of number of records can give more accurate outcome and deeply question analysis of the neuropsychological tests can give elaborate results.

REFERENCES

Books

Fischer, J. S., Hannay, H. J., Loring, D. W., & Lezak, M. D.(2004). Observational methods, rating scales and inventories. In M. D. Lezak, D. B. Howieson, & D. W. Loring (Eds.), Neuropsychological assessment (4th ed.). New York: Oxford University Press. 2004. *Observational methods, rating scales and inventories.* 4th. New York: Oxford University Press.

Kononenko, Igor. 1994. Estimating attributes: Analysis and extensions of RELIEF. *Machine Learning: ECML-94* içinde, düzenleyen: Raedt L Bergadano F, 171-182. Catania: Springer Berlin Heidelberg.

Witten IH, Frank E. 2005. *Data Mining: practical machine learning tools and techniques.* San Fransisco: Morgan Kaufmann Publishers.

Strauss, E., Sherman, E. M. S., Spreen, O. 2006. *A compendium of neuropsychological tests.* 3th. New York: Oxford University Press.

Periodic Publications

Ashford JW, Mortimer JA. 2002. Non-familial Alzheimer's disease is mainly due to genetic factors. *J Alzheimers Dis* **169** (7): 4.

Ashraf M., Le K., Huang X. 2010. Information gain and adaptive neuro-fuzzy inference system for breast cancer diagnoses. *Computer Sciences and Convergence Information Technology (ICCIT)* **5**: 911-915.

Bennett DA, Schneider J, Tang Y, Arnold E, Wilson RS. 2006. The effect of social networks on the relation between Alzheimer's disease pathology and level of cognitive function in old people: a longitudinal cohort study. *Lancet Neurol* **406** (12): 5.

Blessed G, Tomlinson B E & Roth M. 1968. The association between quantitative measures of dementia and of senile change in the cerebral grey matter of elderly subjects. *Brit. J. Psychiat.* **797** (811): 114.

Brink T. L., Yesavage J. A., Lu m, O., Heersema P.H., Adey M., Rose T. S. 1982. Screening tests for geriatric depression rating scale administrered by telephone. *Journal of the American Geriatrics Society* **43**: 674-679.

Brookmeyer R, Johnson E, Ziegler-Graham K, Arrighi H.M. 2007. Forecasting the global burden of Alzheimer's disease. *Alzheimer's & Dementia* **3** (3): 186-191.

Burke, W. J., Roccaforte,W. H.,Wengel, S. P., Conley, D. M., & Potter, J. F. 1995. The reliability and validity of the geriatric depression rating scale administered by telephone. *Journal of the American Geriatrics* **43**: 647-649.

Clark CM, Davatzikos C, Borthakur A, Newberg A, Leight S, Lee VM, et al. 2008. Biomarkers for early detection of Alzheimer pathology. *Neurosignals* **11** (8): 16.

Cortes F., Nourhashe´mi F., Gue´rin O., Cantet C., Gillette-Guyonnet S., Andrieu S., et al. 2008. Prognosis of Alzheimer's disease today: A two-year prospective study in 686 patients from the REAL-FR study. *Alzheimer's and Dementia* **4** (1): 22-29.

Del Sole A, Clerici F, Chiti A, Lecchi M, Mariani C, Maggiore L, et al. 2008. Individual cerebral metabolic deficits in Alzheimer's disease and amnestic mild cognitive impairment: an FDG PET study. *Eur J Mucl Med Mol Imag* **1357** (66): 35.

Dooneief, G., Marder, K., Tang, M. X., & Stern, Y. 1996. The Clinical Dementia Rating Scale: community-based validation of 'profound' and 'terminal' stages. *Neurology* **46**: 1746-1749.

Dubois B, Feldman HH, Jacova C, Cummings JL, Dekosky ST, Barberger-Gateau P, et al. 2010. Revising the definition of Alzheimer's disease: a new lexicon. *Lancet Neurol* **1118** (27): 9.

Eastwood M. R., Lautenschlaegar E., Corbin S. 1983. A comporison of clinical methods for assessing dementia. *Journal of the American Geriatrics Society* **3**: 267-273.

Farrer LA, Cupples L, Haines JL, et al. 1997. Effects of Age, Sex, and Ethnicity on the Association Between Apolipoprotein E Genotype and Alzheimer Disease: A Meta-analysis. *JAMA* **1349** (1356): 278(16).

Folstein M, Folstein S, McHugh PR. 1975. Mini-metal state: a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res.* **189** (198): 12.

Folstein MF, Folstein SE, McHugh PR. 1975. Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research* **3** (12): 98-189

Fowler KS, Saling MM, Conway EL, Semple J, Louis WJ. 1997. Computerized neuropsychological tests in the early detection of dementia: prospective findings. *J Int Neuropsychol Soc* **139** (46): 3.

Frisoni GB, Weiner MW. 2010. Alzheimer's disease neuroimaging initiative special issue. *Neurobiol Aging* **1259** (62): 31.

Gauthier S, Reisberg B, Zaudig M, et al. 2006. Mild cognitive impairment. *Lancet* 1262 (70): **367** (9518).

Group, Canadian Study of Health and Aging Working. 1994. *Canadian Study of Health and Aging: study methods and prevalence of dementia.* **150**, 899–913. Can Med Assoc J.

Gungen C, Ertan T, Eker E, et al. 1999. The standardized Mini-Mental State Examination in Turkish. Vancouver, Canada: 9th Congress of International Psychogeriatric Association.

Holte C. 1993. Very simple classification rules perform well on most commonly used datasets. *Machine Learning* **11**: 63-91.

Hughes, C. P., Berg, L., Danziger, W. L., Coben, L. A., & Martin, R. L. 1982. A new clinical scale for the staging of dementia. . *British Journal of Psychiatry* **140**: 556-572.

Ikonomovic MD, Klunk WE, Abrahamson EE, Mathis CA, Price JC, Tsopelas ND, et al.. 2008. Post-mortem correlates of in vivo PiB-PET amyloid imaging in a typical case of Alzheimer's disease. *Brain* **1630** (45): 131.

Jang, J. 1993. ANFIS: Adaptive network-based fuzzy inference systems. *IEEE Trans Syst Man Cybern* **23**; 665-685

Katzman R, Brown T, Fuld P, Peck A, Schechter R, Schimmel H. 1983. Validation of the short orientationmemory- concentration test of cognitive impairment. *Am J Psychiatry* **140;** 734 - 739.

Kaufman, D. M. 1991. *Clinical neurology for psychiatrists* . 5th. Philadelphia: Saunders.

Kivipelto M, Ngandu T, Laatikainen T, Winblad B, Soininen H, Tuomilehto J. 2006. Risk score for the prediction of dementia risk in 20 years among middle aged people: a longitudinal, population-based study. *Lancet Neurol* **735** (41): 5.

LA, Zadeh. 1965. A general approach to rule aggregation in fuzzy logic control. *Appl Intelligence* **2**: 333-351.

Leung KK, Barnes J, Modat M, Ridgway GR, Bartlett JW, Fox NC, et al. 2010. Brain MAPS: an automated, accurate and robust brain extraction technique using a template library. *Neuroimage* **1316** (25): 49.

Lobo A, Launer LJ, Fratiglioni L, et al. 2000. Prevalence of dementia and major subtypes in Europe: a collaborative study of population-based cohorts. *Neurology* **54** ((suppl 5):): 4–9.

Lynch C., Walsh C., Blanco A., Moran M., Coen R., Walsh J., et al. 20006. The clinical dementia rating sum of box score in mild dementia. *Dementia and Geriatric Cognitive Disorders* **21** (1): 40-43.

McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. 1984. , Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's disease. *Neurology* **939** (44).

Michael W. Weiner, Dallas P. Veitch, Paul S. Aisen, Laurel A. Beckett, Nigel J. Cairns, Robert C. Green, Danielle Harvey, Clifford R. Jack, William Jagust, Enchi Liu, John C. Morris, Ronald C. Petersen, Andrew J. Saykin, Mark E. Schmidt, Leslie Shaw, Judi. 2012. Alzheimer's Disease Neuroimaging Initiative, The Alzheimer's Disease Neuroimaging Initiative: A review of papers published since its inception. *Alzheimer's & Dementia* **8** (1): S1-S68.

Morris J.C. 1993. The Clinical Dementia Rating (CDR): current version and scoring rules. *Neurology* **43** (11): 2412-2414.

Morris, J. 1997. Clinical Dementia Rating: A Reliable and Valid Diagnostic and Staging Measure for Dementia of the Alzheimer Type. *International Psychogeriatrics* **173** (176): 9.

Myers AJ, Goate AM. 2001. The genetics of late-onset Alzheimer's disease. *Curr Opin Neurol* **433** (40): 14.

Nordlund A, Toldysf D, Hellstrom P, Sjogren M, Hansen S, Wallin A. 2005. The Goteborg MCI study: mild cognitive impairment is a heterogeneous condition. *J Neurol Neurosurg Psychiatry 2005;76(11):1485-90.* 1485 (90): **76** (11).

Pal K, Mitra S. 1992. Multilayer Perceptron, Fuzzy Sets, and Classification. *IEEE Transacions on Neural Networks* **3** (5).

Petersen RC, Roberts RO, Knopman DS, Boeve BF, Geda YE, Ivnik RJ, et al. 2009. Mild cognitive Impairment: ten years later. *Arch Neurol* **1447** (55): 66.

Quinlan R. 1986. Induction of Decision Trees. *Mach. Learn* **1** (1): 81-106.

Reisberg B, Ferris S. H., Leon M. J., Crook T. 1982. The Global Deterioration Scale for assessment of primary degenerative dementia. *The American Journal of Psychiatry* **139** (9): 1136-1139.

Ruck W, Rogers K, Kabrisky M, Oxley E, Suter B. 1990. The Multilayer Perceptron as an Approximation to a Bayes Optimal Discriminant Function. *IEEE Transacions on Neural Networks* **1** (4).

Ruck W, Rogers S, Kabrisky M. 1989. Feature Selection Using a Multilayer Perceptron. *Journal of Neural Network Computing* **2** (2): 40-48.

Ruitenberg A, Ott A, Swieten J, Hofman A, Breteler M. 2001. Incidence of dementia: does gender make a difference? *Neurobiology of Aging* **22** (4): 575-580.

Sluimer JD, Bouwman FH, Vrenken H, Blankenstein MA, Barkhof F, van der Flier WM, et al. 2008. Whole-brain atrophy rate and CSF biomarker levels in MCZI and AD: a longitudinal study. *Neurobiol Aging* **8**.

Stern Y., Mayeux R., Sano M., Hauser W. A., Bush, T. 1987. Predictors of disease course in patients with probable Alzheimer's disease. *Neurology* **37** (10): 1649-1653.

Sugeno M, Kang GT. 1988. Structure identification of fuzzy model. *Fuzzy Sets Syst* **28** (1): 15-33.

Takagi T, Sugeno M. 1985. Fuzzy identification of systems and its application to modeling and control. *IEEE Trans Syst Man Cybern* **116** (132): 15(1).

Walker P, Smith B, Liu Q, Famili A, Valdes J, Liu Z, Lach B. 2004. Data Mining of gene expression changes in Alzheimer brain. *Artificial Intelligence in Medicine* **137** (154): 31.

Wilson RS, Scherr PA, Schneider JA, Tang Y, Bennett DA. 2007. Relation of cognitive activity to risk of developing Alzheimer disease. *Neurology* **1911** (20): 69.

Yesavage JA, Brink TL, Rose TL, et al. 1983. Development and validation of a geriatric depression screening scale: a preliminary report. *J Psychiatr Res.* **37** (49): 17.

Yesavage, J. A., Brink, T. L., Rose, T. S., Lum, O., Huang, V., Adey, M. B., et al. 1983. Development and validation of a geriatric depression rating scale: A preliminary report. *Journal of Psychiatric Research* **17**: 37-49.

APPENDICES

APPENDIX-1, MMSE

MİNİ MENTAL DURUM MUAYENESİ
(MMSE)

Adı Soyadı : **Prot. No. :** **Tarih : ..... / ..... / 20.....**

PUAN ☐

ORYANTASYON

Zaman ☐

☐ Yıl :
☐ Ay :
☐ Tarih :
☐ Gün :
☐ Mevsim :

Mekan ☐

☐ Ülke :
☐ Kent :
☐ Hastane :
☐ Bölüm :
☐ Kat :

KAYIT ☐

☐ Mavi ☐ Şahin ☐ Lale

DİKKAT ☐

100 ..... ☐ ..... ☐ ..... ☐ ..... ☐ ..... ☐

A ☐ Y ☐ N ☐ Ü ☐ D ☐

HATIRLAMA ☐

☐ Mavi ☐ Şahin ☐ Lale

APPENDIX-1, MMSE

DİL ☐

ADLANDIRMA

Kalem ☐ Saat ☐

TEKRARLAMA

" O gelmiş olsaydı ben de giderdim" ☐

ANLAMA

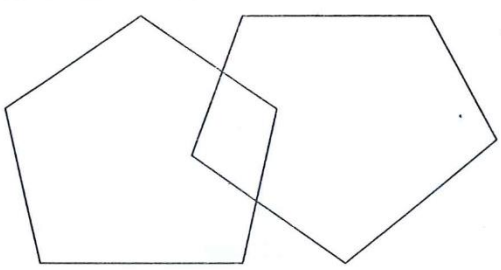
Kağıdı elinize alın, ☐ ortadan ikiye katlayın, ☐ ayağınızın dibine bırakın, ☐

YAZI ☐

OKUMA ☐

GÖZLERİNİZİ KAPAYIN

KOPYA ☐



APPENDIX-2, GDS

GLOBAL BOZULMA ÖLÇEĞİ (GDS)

Adı Soyadı : Tarih : ..... / ..... / .....

Hasta Yakını : Prot. :

1- Bellek kusuruna ilişkin yakınma yok
Klinik görüşme ile bellek kusuru saptanmıyor.

2- Bellek kusuruna ait, özellikle aşağıda sıralanan alanlarda yakınmalar var:
a) Eşyalarını koyduğu yerleri unutuyor,
b) Önceden iyi bildiği isimleri unutuyor.
Klinik görüşmede bellek kusuruna ait normal bir kanıt yok
İş ve toplumsal ortamlarda nesnel bir bozukluk yok.
Semptomatolojiye yönelik uygun düzeyde endişe taşıyor.

3- En erken gösterilebilir bozukluk bulguları.
Aşağıdaki alanlarda birden fazla bulgu :
a) İyi bilmediği çevrelere gittiğinde kayboluyor.
b) İş arkadaşları, hastanın bozulmaya yüz tutan çalışma performansının farkındalar
c) Kelime ve işim bulma güçlükleri yakınları tarafından fark ediliyor.
d) Bir kitap ya da yazıyı okuduğunda eskisi gibi hatırında kalmıyor.
e) Yeni tanıştığı insanların isimlerini hatırlamakta güçlüğü var
f) Değerli bir nesne kaybedilmiş ya da konulmaması gereken bir yere konmuş.
g) Konsantrasyon eksikliği klinik testler sırasında aşikar.
Bellek bozukluğuna ilişkin, ancak yoğun bir görüşmeden sonra ortaya konulabilen normal bulgular
Uğraşı gerektiren iş koşulları ya da toplumsal ortamlarda düşük performans.
Hastada inkar mekanizması belirgin hale gelir olmuş.
Belirtilen ılımlı ya da orta düzeyde bir anksiyete eşlik edebilir.

4- Dikkatli bir klinik görüşme sonrasında ortaya konulan aşikar bozukluk bulguları
Bozukluk aşağıdaki alanlarda ortaya konuyor :
a) Günlük ve yakın geçmişe ait olaylara ilişkin bilgide azalma
b) Kişisel geçmişe ait bazı bellek problemleri.
c) Çıkarma dizileriyle ortaya konulan konsantrasyon bozukluğu
d) Yolculuk yapma, para işleriyle uğraşma gibi yeteneklerde azalma
Aşağıdaki alanlar genellikle sorunsuz
a) Yer ve zaman oryantasyonu
b) Bildik kişi ve yüzlerin tanınması
c) Bilinen yerlere yolculuk yapabilme.
Karmaşık işlevlerin yerine getirilemez olması
Baskın savunma mekanizması olarak inkar kullanılıyor.
Duygulanımda küntleşme ve sıkıntı yaratan durumlardan kaçınma.

5- Yaşamlarını sürdürebilmeleri için yardım gerekmektedir.
Hasta güncel yaşamına ilişkin temel özelliklerden birini hatırlayamıyor. Örneğin:
a) Yıllardır kullanmakta olduğu adres ya da telefon numarasını.
b) Yakın aile üyelerinin isimlerini (torunları gibi)
c) Mezun olduğu lise ya da yüksek okulun adını.
Zaman (gün, haftanın günü, mevsim, v.b.) ya da oryantasyonunda bozulmalar
Eğitimli bir kişi, 40'tan geriye 4'er, ya da 20'den geriye 2'şer saymakta gülük çekebilir.
Bu evredeki kişiler kendilerine ve diğerlerine ait temel gerçeklere ait bilgiyi korurlar.
Kendi isimlerini daima, eş ve çocklarınınkileri genellikle bilirler.
Temizlenmek ve yemek yemekte yardım gerekmez, ancak uygun giysiyi seçmekte güçlükleri olabilir.

6- Bazen, yaşamlarını sürdürmek için tümüyle bağımlı oldukları eşlerinin ismini unutabilirler
Yaşamlarındaki yakın geçmişe ilişkin olay ve deneyimlerinin tümünden büyük ölçüde habersizdirler.
Çevreye ilişkin bazı bilgiler korunabilir, yıl , mevsim, v.b.
10'dan geriye, bazen de ileriye doğru 1'er saymakta güçlükleri olabilir.
Günlük yaşam aktivitelerinde yardım gerekir.

APPENDIX-2, GDS

a) İdrar inkontinansı olabilir.
b) Yolculuk için yardım gerekir, fakat bazen bildik yerlere gidebilirler.
Diurnal ritm sıklıkla bozulmuştur.
Hemen daima kendi isimlerini hatırlarlar
Genellikle, çevrelerindeki tanıdık kişileri yabancılardan ayırabilirler.
Kişilik ve emosyon değişiklikleri görülür. Bunlar oldukça değişkendir ve şunları içerir:
a) Hezeyan davranış, örn., eşlerini taklit olmakla suçlayabilirler; çevredeki hayali kişilerle, ya da aynadaki kendi imgeleriyle konuşabilirler.
b) Obsesif belirtiler olabilir, örn., hasta sürekli olarak basit bir temizlik hareketini tekrarlayabilir.
c) Anksiyete belirtileri, ajitasyon ve daha önce mevcut olmayan tarzda bir saldırganlık görülebilir.
d) Kongitif abuli, örn., amaca yönelik bir davranışın uygulanması için gerekil düşüncenin yeterli süre taşınamaması nedeniyle irade gücünün kaybı.

7- Bu evre süresinde tüm verbal yetenekler kaybedilir.
Bu evrenin erken döneminde bazı kelime ve cümleler söylenebilsede konuşma son derece sınırlanmıştır.
Evrenin ilerlemesiyle, homurdanmak dışında, konuşma tümüyle yitirilir.
İdrar inkontinansı ve yemek yemek için yardım gerekir.
Temel psikomotor yetenekler (örn. yürümek) evrenin ilerlemesiyle kaybedilir.
Beyin bedene ne yapması gerektiğini söyleme yeteneğini artık yitirmiş gibidir.
Genel ve kortikal nörolojik bulgu ve belirtiler bu evrede genellikle mevcuttur.

APPENDIX-3, CDR AND CDR - SB

KLİNİK DEMANS EVRELEME ÖLÇEĞİ (CDR)

Adı Soyadı :

Tarih : ..... / ..... / .....

Hasta Yakını :

Prot. :

Evre .....

1. Bellek

0- Bellek kaybı yok yada hafif ve belirsiz unutkanlık ☐

0.5 Hafif fakat aşikar unutkanlık; olayların kısmen hatırlanabilmesi; "selim" unutkanlık ☐

1- Orta düzeyde unutkanlık, yakın dönem olayları için daha belirgin; unutkanlık günlük aktiviteleri etkiliyor. ☐

2- Ağır düzeyde unutkanlık; yalnızca çok iyi öğrenilmiş materyal tutulabilir; yeni materyal hızla yitirilir. ☐

3- Ağır düzeyde unutkanlık; yalnızca parçacıklar kalır ☐

2. Oryantasyon

0- Tümüyle oryante ☐

0.5 Zaman ilişkilerinde hafif güçlük dışında tümüyle oryante ☐

1- Zaman ilişkilerinde orta derecede güçlük; muayenede mekana oryante; dışarıda coğrafi disoryantasyonu olabilir ☐

2- Zaman ilişkilerinde ağır düzeyde güçlük; genellikle zamana, sıklıkla da mekana disoryante ☐

3- Yalnızca kişilere oryante ☐

3. Yargılama ve Problem Çözme

0- Günlük problemler ve çalışma hayatı ve mali işlerle ilgili problemleri iyi çözer ☐

0.5- Problem çözme, benzerlik ve farklılıkları kavramakta hafif bozukluk ☐

1- Problem çözmek, benzerlik ve farklılıkları halletmekte orta düzeyde bozukluk; toplumsal yargılama genellikle korunmuştur. ☐

2- Problem çözmek, benzerlik ve farklılıkları halletmekte ağır düzeyde bozukluk; genellikle toplumsal yargılama da bozuktur. ☐

3- Yargılama ve problem çözme tümüyle bozuk. ☐

4. Ev Dışında İşlevsellik

0- İşin, alışverişin, gönüllü gruplar ve toplumsal gruplar içinde her zamanki düzeyde bağımsız işlevsellik ☐

0.5- Anılan aktivitelerde hafif bozulma ☐

1- Anılan aktivitelerden bazılarını halen sürdürse de, bağımsız işlev görememe; yüzeysel bir bakışla hala normal görünebilir. ☐

2- Ev dışında bağımsızlığını tümüyle yitirmiş / Ev dışında aktivitelere götürülebilecek kadar iyi görünür. ☐

3- Ev dışında bağımsızlığını tümüyle yitirmiş / Ev dışında aktivitelere götürülemeyecek kadar hasta görünür. ☐

5. Ev Yaşamı ve Hobiler

0- Ev yaşamı, hobiler ve entellektüel ilgiler iyi korunmuş ☐

0.5- Ev yaşamı, hobiler ve entellektüel ilgilerde hafif bozulma ☐

1- Evdeki işlevlerde hafif fakat aşikar bozulma; güç ev işleri, karmaşık hobiler ve ilgiler fark edilmiş durumda ☐

2- Yalnızca basit işler yapabiliyor; ilgiler son derece sınırlı ☐

3- Evde kayda değer bir işlevselliği yok ☐

6. Kişisel Bakım

0- Kendine bakıma tümüyle muktedir ☐

1- Gayrete getirilmesi gerekiyor ☐

2- Giyinme, hijyen ve diğer kişisel bakım için yardım gerekiyor ☐

3- Kişisel bakım için önemli ölçüde yardım gerekir, genellikle enkontinandır. ☐

APPENDIX-3, CDR AND CDR - SB

EVRELEME

Eğer en az ü kategorinin puanı, bellek kategorisi üstünde ya da altında değilse, evre bellek puanıyla aynıdır, böyle bir durumda ise, evre o üç kategorinin puanıyla anıdır. Bunun tek istisnası olarak, üç kategorinin puanı, bellek puanının bir tarafında, diğer iki kategorininki ise diğer tarafında ise evre bellek puanıdır. Bellek puanı 0.5 ise evre 0 olamaz, diğer kategorilerin puanına bağlı olarak 0.5 ya da 1 olmalıdır. Bellek puanı 0, fakat en az iki kategori 1 ya da daha fazla ise evre 0.5 olmalıdır.

CDR EVRELEMESİ İÇİN GEREKLİ SORULAR

HASTA YAKINI SORULARI

1- BELLEK
- Hastanın belleğiyle ilgili sorunları var mı? Varsa sürekli mi? Günlük yaşamını etkiliyor mu? Geçen yıl içinde kötüleşti mi? Örnek verin.
- Kısa bir alışveriş listesini hatırlayabilir mi?
- Kısa süre önce olanları hatırlayabiliyor mu?
- Uzak geçmişe ait olanlara ne dersiniz (doğum günleri, yıl ddönümleri, çalıştığı yerler, eski arkadaşlar gibi)?
- Olayların ayrıtnılarını hatırlayabiliyor mu?
- Geçen hafta ya da ay içinde her zamankinden farklı bir şey yaptı ya da yaşadı mı? Bana biraz ayrıntı verirseniz, ne kadar hatırladığını ona soracağım.
- Nerde doğdu? Doğum günü nedir?
- İlkokula nerde gitti? Okulunun adı nedir?

2- ORYANTASYON
- Mahalle içinde ya da daha uzak çevrede yolunu bulabiliyor mu?
- Evde odaları karıştırdığı oluyor mu?
- Günün tarihinden haberdar mıdır?

3- YARGILAMA ve PROBLEM ÇÖZME
- Para çekip çevirebiliyor mu?
- Evde basit tamirat yapabiliyor mu?
- Evde acil durum olsa başa çıkabilir miydi?
- Sosyal ortamda uygunsuz davrandığı oluyor mu?

4- EV DIŞINDA İŞLEVSELLİK
- Son çalıştığı iş neydi?
- Neden emekli oldu?
- Ev dışında araba kullanmak, dostlarla görüşmek, alışveriş gibi bir aktivitede bulunuyor mu?

5- EV YAŞAMI VE HOBİLER
- Meraklı olduğu şeylere ilgisi sürüyor mu? Örn. mutfak işleri, dikiş-nakış, bahçe işleri gibi.
- Halen yapabildiği neler var?

6- KİŞİSEL BAKIM
- Günlük yaşamda kendine bakmaya muktedir mi?
- Bazı şeyler için uyarılması gerekiyor mu?
- Giyinme, yıkanma ve kişisel bakımda yardım gerekiyor mu?

HASTAYA SORULAR

1- BELLEK
- Bana geçen hafta ya da ay içinde yaptığınız ya da yaşadığınız her zamankinden farklı bir olayı anlatır mısınız (Kimler vardı, hangi nedenle gibi)?
- Son olarak nerde çalışıyordunuz?
- Neden emekli oldunuz?
- İlkokula nerde gittiniz? Adı neydi?
- Nerde büyüdünüz?
- Doğum yeriniz ve tarihini söyler misiniz?
- Yatak başı bellek testleri kullanabilirsiniz.

2- ORYANTASYON
- MMSE oryantasyon sorularını kullanın

3- YARGILAMA ve PROBLEM ÇÖZME

Size şimdi iki ayrı şeyin arasında ne ortak özellik olduğunu soracağım. Örneğin, bir ağaç bir çiçek, her ikisi de bitkidir.

- Elma ile portakal arasında ne ortak özellik vardır?
- Masa ile sandalye arasında ne ortak özellik vardır?
- Resim ile müzik arasında ne ortak özellik vardır?
- Yakın bir arkadaşınızın yaşadığını bildiğiniz sizin için yabancı bir şehre gitseniz ne yapardınız?
- Tanesi 75 bin liradan üç bilet aldınız. 250 bin lira verdiniz. 250 bin lira verdiniz. Ne kadar para üstü alırsınız?

APPENDIX-4, GerDS

GERİYATİK DEPRESYON ÖLÇEĞİ

(Hasta Görüşmesi ile)

Adı Soyadı :

Hasta Yakını :

Tarih : ..... / ..... / .....

Prot. :

Son bir hafta içinde kendinizi nasıl hissettiniz? Aşağıdaki soruları buna göre cevaplayın.

PUAN :

	EVET	HAYIR
1. Genel olarak hayatınızdan memnun musunuz ?	☐	☐
2. Günlük uğraşı ve ilgilerinizin büyük bölümünü terkettiniz mi ?	☐	☐
3. Yaşantınızın boş olduğunu düşünüyor musunuz ?	☐	☐
4. Sıkılıyor musunuz?	☐	☐
5. Gelecekten umutlu musunuz ?	☐	☐
6. Kafanızdan uzaklaştıramadığınız düşünceler nedeniyle endişeli misiniz?	☐	☐
7. Ruh haliniz genelde iyi mi?	☐	☐
8. Başınıza kötü bir şey geleceğinden endişe ediyor musunuz?	☐	☐
9. Kendinizi genelde mutlu hissediyor musunuz ?	☐	☐
10. Kendinizi sık sık çaresiz hissediyor musunuz?	☐	☐
11. Kendinizi sık sık huzursuz ve yerinde duramaz hissediyor musunuz?	☐	☐
12. Dışarıya çıkıp yeni bir şeyler yapmak yerine, evde oturmayı mı tercih ediyorsunuz ?	☐	☐
13. Sık sık gelecekten kaygı duyuyor musunuz?	☐	☐
14. Hafıza ile ilgili sorunlarınızın çoğu kişiden daha fazla olduğunu düşünüyor musunuz?	☐	☐
15, Şu anda hayatta olmanın harika bir şey olduğunu düşünüyor musunuz?	☐	☐
16. Kendinizi sık sık kederli ve hüzünlü hissediyor musunuz?	☐	☐
17. Kendinizi değersiz hissediyor musunuz?	☐	☐
18. Geçmiş üzerine çok mu kaygılanıyor sunuz?	☐	☐
19. Hayatı heyecan verici buluyor musunuz?	☐	☐
20. Yeni tasarılara başlamak sizin için güç müdür?	☐	☐
21. Kendinizi enerji dolu hissediyor musunuz?	☐	☐
22. Durumunuzu ümitsiz görüyor musunuz?	☐	☐
23. Çoğu kişinin sizden daha iyi durumda olduklarını düşünüyor musunuz?	☐	☐
24. Küçük şeyler sizi kolaylıkla küstürüyor mu?	☐	☐
25. Sık sık ağlama hissi duyuyor musunuz?	☐	☐
26. Konsantre olmakta güçlük çekiyor musunuz?	☐	☐
27. Sabahları uyanmaktan zevk alıyor musunuz?	☐	☐
28. İnsanlarla birlikte olmaktan kaçıyor musunuz?	☐	☐
29. Karar vermekte güçlük çekiyor musunuz?	☐	☐
30. Zihniniz eski berraklığında mı?	☐	☐

APPENDIX-5, BOMC

BLESSED KISA ORYANTASYON - BELLEK KONSANTRASYON TESTİ

(Her yanlışa 1 puan verin)

Adı Soyadı : **Prot.:** **Tarih : ..... / ..... / .....**

MADDELER	**Hasta Puan**		**Ağırlık**	
1. Hangi yıldayız ?	1	x	4	= .....
2. Hangi aydayız ?	1	x	3	= .....

Söyleyeceğim adresi aklınızda tutun :

Emine Keskin
Fırın sok. No.: 42
Bartın

3. Şu anda saat yaklaşık kaçtır? (1 saat içinde)	1	x	3	= .....
4. Yirmiden geriye doğru birer birer sayın	2	x	2	= .....
5. Ayları geriye doğru sayın	2	x	2	= .....
6. Daha önce söylediğim adresi tekrarlayın	5	x	2	= .....

Toplam = ...

APPENDIX-6, BDRS

BLESSED DEMANS DERECELENDİRME ÖLÇEĞİ
(BDRS - CERAD Versiyonu)

Hasta Adı Soyadı :

Hasta Yakını :

Tarih : ..... / ..... / .....

Değerlendiren :

Bellek ve Günlük Aktivitelerde Performans

Alt Skor :

	YETENEK	Kayıp
1.	Ev işleriyle uğraşma yeteneği	
2.	Para çekip çevirebilme yeteneği	
3.	Kısa bir malzeme listesini hatırlama yeteneği (örn. alışveriş listesi)	
4.	Evde yolunu bulma yeteneği (kendi evi veya diğer tanıdık mekanlar)	
5.	Sokakta bildik mekanlarda yönünü bulma yeteneği	
6.	Olayları veya açıklamaları kavrayabilme yeteneği	
7.	Yakın geçmişe ait olayları hatırlayabilme yeteneği	
8.	Geçmişte yaşama eğilimi	

0	Yok
0.5	Hafif
1	Ağır

Alışkanlıklar

Alt Skor

	ALIŞKANLIK	GEREKLİ YARDIM DÜZEYİ
9.	**Yemek Yeme** 0 Yardımsız yemek yiyebiliyor 1 Biraz yardımla yemek yiyebiliyor 2 Yemekte oldukça yardım gerekiyor 3 Yedirilmesi gerekiyor	
10.	**Giyinme** 0 Yardımsız 1 Bazen düğmeleri karıştırabiliyor. Vb. biraz yardım gerekiyor 2 Yanlış sırayla giyiniyor bazı giysileri unutabiliyor oldukça yardım gerekiyor 3 Giydirilmesi gerekiyor	
11.	**Tuvalet** 0 Temiz kalabiliyor, tuvalet sorunsuz 1 Seyrek inkontinans veya hatırlatılması gerekiyor 2 Sık inkontinans veya oldukça yardım gerekiyor 3 Sfinkter kontrolü yok	

Toplam BDRS Skoru :