Classification and treatment of different stages of Alzheimer’s disease using various machine learning methods

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Abstract: There has been a steady rise in the number of patients suffering from Alzheimer’s disease (AD) all over the world. Medical diagnosis is an important but complicated task that should be performed accurately and efficiently and its automation would be very useful. The patient’s records are collected from National Institute on Aging, USA. The Sample consisted of initial visits of 496 subjects seen either as control or as patients. Patients were concerned about their memory at the National Institute on Aging. It also consisted of patients and caregiver interviews. This research work presents different models for the classification of different stages of Alzheimer’s disease using various machine learning methods such as Neural Networks, Multilayer Perceptron, Bagging, Decision tree, CANFIS and Genetic algorithms. The classification accuracy for CANFIS was found to be 99.55% which was found to be better when compared to other classification methods. Based on the outcome of classification accuracies, various management and treatment strategies such as pharmacotherapeutic and non pharmacotherapeutic interventions for mild, moderate and severe AD were elucidated, which can be of enormous use for the medical professionals in diagnosis and treatment of AD.

Keywords: Alzheimer’s Disease, Neural Networks, Multilayer Perceptron, Bagging, Decision tree, CANFIS and Genetic Algorithms, Pharmacotherapeutic intervention, Non-Pharmacotherapeutic intervention

Introduction
Alzheimer’s disease is a progressive neurodegenerative brain disorder that is slow in onset but leads to dementia, unusual behavior, personality changes and ultimately death [1]. The personality distortions interfere with the patient’s professional life, social activities and relationships [2]. It is a chronic, progressive disabling organic brain disorder characterized by disturbance of multiple cortical functions, including memory, judgment, orientation, comprehension, learning capacity and language [3]. The most common cause of dementia in the elderly is probably Alzheimer’s disease (AD) [4]. The National Institute of Health predicts, if the current trend continues, there will be more than 8.5 million AD patients by the year 2030 in the USA alone [5]. Alzheimer’s disease (AD) was first described by the German psychiatrist, Alois Alzheimer, in 1907. The disease appeared less common in the early decades of the 20th century. Although there are a number of medical areas to which Machine Learning (ML) systems have been applied, dementia has not been one of them. Yet AD is a complex problem with correct diagnosis requiring historical data, physical exam, cognitive testing, laboratory investigations etc. Although diagnostic accuracy using clinical NINCDS-ADRSA criteria for probable AD is about 88% compared to post-mortem diagnosis [6] most demented patients with AD are seen by community physicians who often do not detect AD or misdiagnose it [7]. This problem is compounded by the average delay of 4 years between symptom onset and first physician contact [8] which usually related to the patient’s social embarrassment about having a memory problem. At this point of the disease, physicians are less able to slow the progression and minimize debilitating behavioral effects of the AD. A simple unobtrusive method for detecting AD early in the disease’s course would help get patients to seek early evaluation and treatment. Early detection and correct diagnosis can lead to disease-retarding therapies which can slow disease progression and reduce patient and caregiver stress and morbidities. At present there are many more classification algorithms for example classification based on decision tree, Bayesian classification etc. But we need to apply such an algorithm to deal with all kinds of neuropsychological tests, mental status examinations and laboratory investigations, by which we will get best possible treatments for AD according to the investigation reports entered in the database and thus we can manage AD very well. The article puts forward the usage of existing Machine learning methods for the classification of different stages of AD as mild, moderate, severe and Normal. The next part of this paper presents the best possible treatment and the management for the various stages of Alzheimer’s disease.

Literature Survey
A detailed study on classification of AD and diagnosis of AD has been proposed by many researchers. This section includes a brief survey of the related work. A method of estimating the
progression rates in Alzheimer’s disease and diagnosis of dementia is presented in [9]. The combination of cognitive testing and an informant questionnaire in screening for dementia is proposed in [10]. Variability in Mini-Mental State Examination score in patients with probable Alzheimer’s disease is presented in [11]. David F. Tang-Wai and David S. Knopman [12] proposed the Comparison of the Short Test of Mental Status and the Mini-Mental State Examination in Mild Cognitive Impairment. Detecting very early stages of dementia from normal aging with machine learning methods proposed by Shankle, WR., Mani, S., Pazzani, M. [13]. A study on the prediction of various diseases using artificial neural networks and genetic algorithms has been proposed by many researchers. Yasuyuki Tomita et al. [14] proposed Artificial Neural Network Model for Prediction of Childhood Allergic Asthma Using Single Nucleotide Polymorphism Data. In order to predict development of disease, they applied a knowledge processing method based on an artificial neural network (ANN) model to diagnostic prediction of 172 subjects with childhood allergic asthma (CAA) and 172 healthy subjects. Prediction of Radiation Induced Liver Disease (RILD) using Artificial Neural Networks was proposed by Ji Zhu et al. [15]. A total of 93 primary liver carcinoma (PLC) patients with single lesion and associated with hepatic cirrhosis of Child–Pugh grade A were treated with hypofractionated three-dimensional conformal radiotherapy (3D-CRT). Eight out of 93 patients were diagnosed RILD. The Prediction of major histocompatibility complex II-Peptide Interaction Using Fuzzy Neural Network is proposed by Hideki Noguchi and Taizo Hanai in [16].

Motivation

Until recently, the most significant issue facing a family physician is the diagnosis and treatment of AD. However, as more treatment options become available, it will become increasingly important to diagnose AD early. Dementia of AD type may be suspected if memory deficits are exhibited during the medical history and physical examination. Information from the patient’s family members, friends and caregivers may also point to signs of AD. Distinguishing age-related cognitive decline, mild cognitive impairment and Alzheimer’s disease may be difficult and requires evaluation of cognitive and functional status. The prevalence of AD is expected to increase dramatically in future years as life expectancy continues to increase and the baby-boomer population ages. The cumulative incidence of Alzheimer’s disease has been estimated to be as high as 4.7 percent by age 70, 18.2 percent by age 80 and 49.6 percent by age 90. Proposed risk factors for AD include a family history of dementia, previous head injury, lower educational level and female sex. Alzheimer’s disease is the most common cause of dementia; many of the remaining cases of dementia are caused by vascular disease and Lewy body disease. Vascular disease and Lewy body disease often occur in combination with Alzheimer’s disease. Hence there is an urgent need to understand the disease, to develop prophylactic strategies which can distinguish the different states of AD, so that the proper step can be taken to manage the disease.

Problem Definition

The sample consists of initial visits of 496 subjects seen either as control or as patients. Patients were concerned about their memory at the National Institute on Aging consists of patients and caregiver interviews. The Neurologists and Neurophysiologists apply the DSM-IV [17] criteria along with some laboratory investigations to classify the subject’s mental status as either normal, cognitively impaired i.e. dementia of Alzheimer’s type. The dataset consists of 35 attributes broadly classified under five main observations namely age, neuropsychiatry assessments, mental status examination and laboratory investigations. Entire description of patient’s data set is shown in the table 1. The first focus of our work is on classification of various stages of Alzheimer’s disease, the next stage proposes the various possible treatments and the management for each stage of AD.

Table 1. Description of Patient’s Dataset

| Observation | Description | Volume |
|-------------|-------------|--------|
| 1. Age      | Age in years | Continuous |
| 2. Neuropsychiatric Assessment | Cognitive Changes, Psychiatric Syndromes, Personality Changes, Behavioural, Family History | Yes/No |
| 3. Mental Status Examination | Mini-Mental Status Examination, Revised Orientation Memory Confrontation, Revised Information Memory Concentration, Clock Test/Memory test | Continuous |
| 4. Physical Investigations | Blood Pressure, Blood Glucose, Urine Chemistry Tests, Physical Testing, Appropriation of Testing, Hematological Screen for Mercury | Continuous |
| 5. Laboratory Investigations | Alzheimer’s Disease, 4 Stages: Normal, Mild, Moderate, Severe | |

Model

The Architecture and modelling of the current paper is depicted in Fig 1. It begins with the collection of patients records, which is followed by preprocessing of data set includes converting the data in to numeric values. Next stage is evaluating the attributes by using gain ratio attribute evaluation scheme with ranker search.
method. The main focus of our work is on classification of various stages of AD using various Machine learning methods. The last and the most important stage is treatment and management of AD, in this stage we suggest different approaches for the management for each of the classified stages of AD.

![Architecture of Classification of Different Stages of Alzheimer's disease](image)

**Collection of Patient’s Records**
The patient’s records are collected from National Institute on Aging, USA. The data set in our study consists of initial visits of 496 subjects seen either as control or as patients. Patients were concerned about their memory at the NIA, consists of patients and caregiver interviews. The neurologists and Neurophysiologists apply the DSM-IV criteria along with some laboratory investigations to classify the subject’s mental status as either normal, cognitively impaired i.e. dementia of Alzheimer’s type. The National Institute on Aging, a component of the National Institutes of Health, USA supports 28 Alzheimer’s disease Centers across the country.

**Pre-Processing Patient’s Records**
In our study most of the collected data is free from outliers, noise and missing data. Some inconsistencies are recorded in the data set these consistencies are corrected manually by using external references.

**Attribute Selection**
Attribute selection involves searching through all possible combinations of attributes in the data to find which subset of attributes works best for prediction and classification. For classification tasks, it can lead to increased accuracy or to reduced computational costs. In the present study we used Gain ratio ranker search method for selecting the attributes.

Gain ratio is defined by the formula:

\[ Gain \text{ ratio} = \frac{\text{Information Gain}}{\text{Split Information}} \]

Where, \( Info \text{ Gain (Class, Attribute)} = H(\text{Class}) - H(\text{Class/Attribute}) \).

Where \( H \) is the information entropy.

**Classification of Diseases**
Classification is the most commonly used data mining technique, which involves the separation of data into segments which are non-overlapping. Classification can be viewed as forecasting a discrete value. Any approach to classification assumes some knowledge about the data. Hence a training set is used to identify specific parameters. Training data requires sample input data, domain expertise, and a classification assignment to the data. In the present study we used five different Machine Learning methods such as Decision tree [18], Bagging [19], Neural Networks, Multilayer Perceptron [20], CANFIS and Genetic Algorithms for the classification of various stages of Alzheimer’s disease.

**Machine Learning (ML)**
Machine Learning and Knowledge Discovery from Databases (KDD) are increasingly being applied in health care to build models, develop practice guidelines or refine guidelines for better medical decision making. They differ from traditional approaches by generating domain models such as decision trees, decision rules, graphs etc. from data. ML methods attempt to learn a description that best separates the different stages of Alzheimer’s disease. As input, each of the initial visits is represented with the attributes described above. The output of each of the learning methods is a representation of the different stages of Alzheimer’s disease that can be applied to classify patients with an unknown Alzheimer’s stage. Each learning method applies a different search technique and concept representation to describe the possible outcomes of the diagnosis. In the proposed system we have applied each of the five ML methods for the classification of different stages of Alzheimer’s disease.

**Neural Networks (NN)**
Neural networks are very sophisticated modelling techniques capable of modelling extremely complex functions. The Neural network is developed based on the human nervous system and the neuron is the fundamental element. A neuron has several inputs and only one output. The neural network consists of three layers 1.Input layer 2.Hidden layer 3.Output layer. The layers are connected with weighted edges. These edges are trained and initialized.

**Multilayer Perceptrons (MLPs)**
Multilayer Perceptrons are feed forward neural networks trained with the standard back propagation algorithm. They are supervised networks so they require a desired response to be trained. They learn how to transform input data into a desired response, so they are widely used for pattern classification. With one or two hidden layers, they can approximate virtually any input-output map. They have been shown to approximate the performance of optimal statistical classifiers in difficult problems. Most neural network applications involve MLPs. This is perhaps the most popular network architecture in use today.

In a Multilayer Perceptron topology neurons are grouped into distinct layers. Output of each layer is connected to input of nodes in the following...
Bagging is a machine learning ensemble meta-
that is expected to contain the best solution.
initial population to evolve towards a population
removal of redundant variables. GAs causes the
generalize on freshly presented data, due to the
less complicated network, with the ability to
training data which can produce a smaller and
useful to select the most relevant features of the
momentum coefficient. This approach also is
parameters such as learning rate, and
of MF for each input, and optimization of control
training and enhance its performance, we use
third layer represents output variables. In order to
(hidden) layer represents fuzzy rules and the
layer represents input variables, the middle
axon. This system can be viewed as a special
function of the particular subclass of the fuzzy
axon. This system can be viewed as a special
two-layer feed forward neural network. The first
layer represents input variables, the middle
(hidden) layer represents fuzzy rules and the
third layer represents output variables. In order to
improve the learning of the CANFIS, quicker
training and enhance its performance, we use
genetic algorithms to search for the best number
of MF for each input, and optimization of control
parameters such as learning rate, and
momentum coefficient. This approach also is
useful to select the most relevant features of the
training data which can produce a smaller and
less complicated network, with the ability to
generalize on freshly presented data, due to the
removal of redundant variables. GAs causes the
initial population to evolve towards a population
that is expected to contain the best solution.

**Bootstrapping aggregating (bagging)**

Bagging is a machine learning ensemble meta-
algorithm to improve machine learning of
classification and regression models in terms of
stability and classification accuracy. Although it is
usually applied to decision tree models, it can be
used with any type of model. Bagging is a special
case of the model averaging approach. In
bagging for each trail t=1,2,3,...T, a training set of
size N is sampled from the original instances.
This training set is the same size as the original
data, but some instances may not appear more
than once. The learning system generates a
classifier C_t from the sample and the final
classifier C* is formed by aggregating the T
classifiers from these trails. To classify an
instance x, a vote for the class k is recorded by
every classifier for which C_t(x) = k and C*(x) is
then the class with the most votes.

**Implementation and performance analysis**

The data set in our study consists of 496 training
cases and 225 testing cases, with 35 attributes
broadly classified under five main observations
namely age, neuropsychiatry assessments,
mental status examination, laboratory
investigations and physical examinations. The
description of the data classification is shown in
table 2. The proposed model begins with
selection of attributes using gain ratio attribute
selection method on the given data set. On the
outcome of the selection method different models
were simulated using various ML methods such as
decision tree, Bagging method, Neural
Network method, Multilayer Perceptron, CANFIS
and Genetic Algorithms for the classification of
different stages of Alzheimer's disease. For the
simulation purpose we have used software's
namely WEKA (Waikato Environment for
Knowledge Analysis) for decision tree and
bagging methods. Matlab software was used for
developing Neural Network and Multilayer
Perceptron model in addition to these the
simulations were realized by using NeuroSolution
software for CANFIS and Genetic Algorithm.

Results of classification accuracies using various
ML methods are shown in table 3. The
classification accuracy for CANFIS was found to
be 99.55% which was found to be better when
compared to other classification methods.
Classification accuracy is almost same for
multilayer Perceptron, but the runtime for
multilayer Perceptron model in addition to these the
simulations were realized by using NeuroSolution
software for CANFIS and Genetic Algorithm.

Results of classification accuracies using various
ML methods are shown in table 3. The
classification accuracy for CANFIS was found to
be 99.55% which was found to be better when
compared to other classification methods.
Classification accuracy is almost same for
multilayer Perceptron, but the runtime for
C4.5 is comparatively higher. The classification
matrix of C4.5 obtained for 225 testing sample
set is shown in table 4. The classification matrix
provides a comprehensive picture of the
classification performance of the classifier. The
ideal classification matrix is the one in which the
sum of the diagonal is equal to the number of
samples. Figure 2 shows the Output Vs Desired
Plot for the test set using CANFIS and genetic
algorithm. Once the classification is done the
next stage would be finding the best possible
treatment and management for Alzheimer's
diseases.
Regular medical management of general health, in addition to monitoring of cognitive deficits, is essential. Management objectives and interventions should be based on psychiatric, neurological and general medical evaluations of the nature and cause of cognitive deficits and associated non-cognitive symptoms. Cholinesterase Inhibitors: These agents are approved for monotherapy as well as combination therapy to improve cognitive functions or delay decline in patients with mild to moderate and severe AD. NMDA (N-methyl-D-aspartate) antagonist: various randomized, placebo - controlled, double blind studies have revealed the efficacy of memantine, the only available NMDA antagonist as a treatment for AD. These have indicated its effects on cognition, activities of daily living and behavior. Antioxidant therapy with Vitamin E etc was found to postpone functional decline. Various natural antioxidant derived from plants were also found be beneficial. Hormonal replacement therapy (HRT) using estrogen was found to delay the onset of AD. (Refer Table 6). AD was found to be associated with various associated behavioral disturbances (mood disorder, apathy, anxiety) which can be managed by using pharmacotherapeutic agents (Table 5). AD patients suffer from behavioral outbreaks such as mood disorder, sleep disorder, irritation, etc which can be managed by adopting simple helpful non-pharmacological strategies (Table 7).

Conclusion
This paper proposes a various models for the classification of different stages of Alzheimer’s disease by considering the different cognitive tests, physical examinations, age, neuropsychiatry assessments, mental status examination and laboratory investigations. The classification accuracy for CANFIS was found to be 99.55% which was better when compared to other classification methods. The classification model was validated with the test cases and the model achieved an average classification accuracy of 99.25%. Based on the outcome of classification accuracies, various management and treatment strategies such as pharmacotherapeutic and non pharmacotherapeutic interventions for mild, moderate and severe AD were elucidated, which can be of enormous use for medical professionals in diagnosis and treatment of AD. It was observed that Donepezil hydrochloride, Galantamine, Rivastigmine tartrate, Rivastigmine, Memantine are the most prescribed drugs for the treatment of Mild, Moderate and Severe Alzheimer’s Disease.

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Table 5- Pharmacotherapy of Alzheimer’s Disease (Stage: Mild and Moderate)

| Pharmacological Treatment of Behavior and Mood (Prescribed Drugs) | Dosage | Comments and cautions |
|-----------------------------------------------------------------|--------|-----------------------|
| **ANTIPSYCHOTICS**                                              |        |                       |
| Aripiprazole (Abilify®)                                        | Initial dose: 5 mg/day (Müller et al., 2007) | Generally classified as non-sedating, weight neutral. Dopamine blocker with agonist properties. Modest documentation. |
| Clozapine (Clozaril®)                                           | Initial dose: 12.5 mg twice daily. Max: 75-150 mg (in divided doses) | Must monitor HbA1c, blood sugar (for possible new onset diabetes) and cholesterol every 3 months. Do not use with bupropion or trazodone (due to increased risk of agranulocytosis). |
| Ziprasidone (Geodon®)                                          | Initial dose: 10 mg/day Max: 80 mg/day Injectable: 20 mg IM (Berkowitz, 2003; Kohen, Preval, Southard, & Francis, 2005) | Should be given with food to increase bioavailability. Generally classified as non-sedating, weight neutral. |
| **MOOD STABILIZERS (ANTI-AGITATION AGENTS)**                    |        |                       |
| Valproate (Depakote®)                                          | Initial dose: 25 mg twice daily. Titrare to maximum of 300 mg daily in divided doses | Monitor liver enzymes, platelets & PT/PTT as indicated. Note: Add lab tests increase cost and discomfort for the patient. For impaired impulse control, aggressive behavior, etc., consider a SSRI. |
| Carbamazepine (Tegretol®)                                      | Initial dose: 125 mg daily. Generally Titrare to Max of 500 mg twice daily although some may go higher | Monitor CBC and liver enzymes regularly. Drug Interactions. Problematic side effects: One controlled study (Tariot et al., 1998). |
| **ANXIOLYTICS — BENZODIAZEPINES**                             |        |                       |
| Lorazepam (Ativan®)                                            | 1 mg of lorazepam = 5 to 10 mg of diazepam oral, sublingual, parenteral | High potency, intermediate acting. Note: Lorazepam is not short-acting and is not safer than other BDZs. The elderly are more sensitive to BDZs than younger patients. |
| Clonazepam (Klonopin®)                                         | 1 mg clonazepam = 1 mg lorazepam | High potency, long acting. Can be useful in BDZ withdrawal. No active metabolite. |
| **ANXIOLYTICS — NON-BENZODIAZEPINES**                          |        |                       |
| Buspirone (Buspar®)                                            | Initial dose: 5 mg twice daily Max: 20 mg three times daily | May be useful in mild-moderate agitation only. May take 2-4 weeks to become effective. Poorly documented efficacy. |
| Zolpidem tartrate (Ambien®)                                    | Non-BDZ sleep med. 5 mg orally at bedtime | Reduced hepatic clearance in the elderly. Amnestic syndrome, sleep walking, hallucinations. |
| **ANTIDEPRESSANTS — TRICYCLICS**                               |        |                       |
| Desipramine (Norpramin®/Pristane®)                            | Initial dose: 10-25 mg daily Max: 150 mg daily | Lower risk for hypotensive and anticholinergic side effects (anticholinergic activity less than paroxetine). May cause tachycardia. |
| Doxepin (Sinequan®/Adapin®)                                    | Initial dose: 10-25 mg at bedtime Max: 150 mg daily | Significant hypothalamic and anticholinergic effects are limiting. |
| Nortriptyline (Aventyl®/Pamelor®)                              | Initial dose: 10 mg at bedtime Max: 100 mg daily | Tolerance profile similar to desipramine but tends to be more sedating. More anticholinergic effects. Moderate sedation may be limiting. |
| **ANTIDEPRESSANTS — HETER- AND NONCYCLICS SELECTIVE SEROTONERGIC REUPTAKE INHIBITORS (SSRIs)** | | General Cautions. These agents may prolong the half-life of other drugs by inhibiting various CYP450 isoenzymes. As a class, typical side effects include sweating, tremors, nervousness, insomnia, orthostasis, dizziness, and various gastrointestinal and sexual disturbances. Withdrawal effects may occur if agents are abruptly discontinued. |
| Citoxetine (Celexa®)                                           | Initial dose: 10 mg daily Max: 40 mg daily | Well tolerated, nausea and sleep disturbances in some. Demonstrated efficacy for treatment of BPDs. |
| Escitalopram (Lexapro®)                                        | Initial dose: 10 mg daily Max: 20 mg/day | Well tolerated, nausea and sleep disturbances in some. |
| Fluoxetine (Prozac®)                                           | Initial dose: 10 mg every other day Max 20 mg daily | Activating. Very long half-life. Side effects may not manifest for a few weeks. |
| Fluvoxamine (Luvox®)                                           | Initial dose: 25 mg daily Max: 100 mg twice daily Reduce by half when using with Cymbalta, Xanax, or Halocid | ———— |
| Cholinesterase Inhibitors (for Treatment of Mild, Moderate and Severe Alzheimer’s Disease) |  |
|---|---|
| Donepezil hydrochloride (Aricept®) | Start: 5 mg daily Escalation: 10 mg daily after 4-6 weeks if tolerated 5 mg dose is effective. Caution when using in people with cardiac conduction conditions such as symptomatic bradycardia, or with a history of falls or syncope (may want to avoid or seek cardiac consult). |
| Galantamine (Razadyne®; Razadyne ER®) | Immediate Release: Start: 4 mg twice daily Escalation: 8 mg twice daily after 4 weeks. May increase to 16 mg twice daily after an additional 4 weeks. Max: 24 mg/day Extended release: Start: 8 mg daily or 4 mg twice daily. Escalation: 16 mg daily after 4 weeks or 8 mg twice daily after 4 weeks. May increase to 24 mg per day (32 mg per day is not more effective in Alzheimer’s Disease). Starting dose is not therapeutic. Maximum dose 16 mg per day if renal impairment Other cautions same as donepezil. |
| Rivastigmine tartrate (Exelon®) | Start: 1.5 mg twice daily Escalation: 3 mg twice daily after 4 weeks. May increase to 4.5 mg twice daily after an additional 4 weeks. May increase to 6 mg twice daily after an additional 4 weeks. Starting dose is not therapeutic. Cautions same as for donepezil and galantamine. |
| Rivastigmine (Exelon®) | Start: 4.5 mg/24 hour patch daily. Escalation: 9.5 mg/24 hour patch daily after 1 month. When switching from oral to the patch: For a total daily dose of less than 6 mg oral rivastigmine switch to 4.5 mg/24 hour patch (first check medication adherence); For a total daily dose between 6-12 mg of oral rivastigmine switch to 9.5 mg/24 hour patch. Apply the first patch on the day following the last oral dose. Starting dose is not therapeutic. Caution same as for donepezil and galantamine. |
| NMDA |  |
| Memantine (Namenda®) | Start: 5 mg daily for 1 week Escalation: 5 mg twice daily for 1 week, then 5 mg and 10 mg in separate doses for 1 week, then 10 mg twice daily Reduce dose in people with renal impairment Target dose of 5 mg BID is recommended in patients with severe renal impairment (creatinine clearance of 5-20 mL/min based on the Cockcroft-Gault equation) |
| ANTI-OXIDANTS |  |
| Vitamin E | not greater than 400 IU per day |
| Estrogen | early studies suggested that estrogen or hormone replacement therapy may delay the onset of Alzheimer’s Disease |
| Ginkgo biloba |  |
**Table 7-Non-pharmacological approaches for the management of associated disorders of Alzheimer’s disease (mild, moderate and severe)**

| Non-pharmacological approaches for Common Behavioral Symptoms and Mood Disorders | Non-Pharmacological Interventions |
|---|---|
| Apathy | Simulation/activities  
Simple tasks like visual, audio, and games |
| Sleep disturbances | Sleep hygiene practices (prayer, bath, meditation)  
Simulation during the day  
Reduction of excessive stimulation/noise (Ex: Noise, TV)  
Light disturbances  
Color management of the room |
| Wandering | Exercise (walking, jogging)  
Alternate therapy (yogasana, pranayama, pranidhana, physiotherapy)  
Safe places to wander  
Visual cues (Photographs, paper slips, carry Personal information) |
| Mood disorders  
Psychotic symptoms | Exercise and pranayama  
Reassurance  
Distraction rather than confrontation  
Removal of potential sources of confusion (e.g., mirrors) |
| Eating/appetite disorders | Offering simple, finger foods  
Removal of distractions from dining area  
Softening music (music therapy)  
Breakdown of tasks into simple steps  
Restriction |
| Irritability/Agitation | |