Grenze International Journal of Engineering and Technology, July 2017

A Research Survey on Alzheimer's Disease

Suresha H.S[1], Dr. S.S.Parthasarathi [2] and Dr. H.S. Sheshadri[3]
[1]Suresha H.S, Associate Professor, Dept of ECE, DBIT, Bangalore, India
srisuri75@gmail.com
[2] Dr. S.S.Parthasarathi , Professor, EEE Dept , PES College of Engineering ,Mandya, India
vsarathypartha@yahoo.com
[3]Dr.H.S. Sheshadri, Professor, ECE Dept, PES College of Engineering, Mandya. India
hssheshadri@gmail.com

***Abstract*—Alzheimer's disease (AD) and dementia in older adults is a major public health problem, the most common cause. The aim of this research article is a brief introduction to AD and mild cognitive impairment (MCI) is to provide the concept. AD and MCI articles that medical students should be familiar with the clinical and neurobiological aspects emphasized. In addition, the use of biomarkers for the diagnosis of articles AD describes progress in ongoing efforts to develop new therapies and highlights.**

Keywords: **Alzheimer's disease, MCI, biomarkers, dementia.**

I. INTRODUCTION

The world's population is aging rapidly, and the number of people with dementia is expected to be in the year to 35 million today to 65 million In 2030 in the United States, 5 million, or 1in 9, more than 65 people living with Alzheimer's (DA), is the most common cause of dementia. By comparison, according to the Center for Disease Control and Prevention (2009-2012 estimates), about 3 million Older adults in the United States, asthma 10 million have diabetes and 20 million have arthritis 25 million have high blood pressure. Primary care physician and older adults with specialists Search dementia is increasing frequency throughout their careers [1]. As dementia has important implications for patients, their families and in our society, it is necessary doctors have a solid understanding of the Subject. The aim of this research article is to provide, a brief introduction to related concepts Mild cognitive impairment (MCI). The research article highlights Clinical and neurobiological aspects of advertising and MCI that medical students should be familiar with. In also, the article describes the use of the advances in AD and highlights ongoing biomarker for the diagnosis of efforts to develop new treatments [2].

II. ALZHEIMER'S DISEASE

German neuropathologist and psychiatrist Dr. Alois Alzheimer's is credited with first describing dementing condition that later became known as AD. In its landmark 1906 convention 1907 Alzheimer described in terms of Auguste D, a "51-year-old woman with the strange disease. The cerebral cortex ", that was Memory loss and speech, disorientation, behavioral symptoms (hallucinations, delusions, Paranoia), and psychosocial. Surprisingly, many of the clinical and pathological observations Alzheimer findings described more than a century, they remain fundamental to our understanding AD today [3].

Grenze ID: 01.GIJET.3.3.68

A. Dementia

Dementia is a clinical syndrome (a group of Signs and symptoms) that included progressive deterioration of intellectual function. Cognitive factors, they can be affected by dementia, including memory, language, reasoning, decision-making, visuospatial function, care and guidance. People with dementia, cognitive disorders often are accompanied changes in personality, emotional regulation, and social behavior. Importantly, behavioral changes that occur with dementia intervention work, social activities and relationships with a person's ability to perform routine daily activities (e.g., driving, shopping, cleaning, cooking, handling finance and personal care)[4]. Table 1 summarizes the diagnostic criteria for all causes of dementia there are many causes reversible and irreversible Madness. Reversible dementias (also referred to as "pseudo-dementia") are relatively rare, but potentially they can be treated and are secondary to another including depression, nutritional deficiencies (For example, vitamin B12), metabolic and endocrine disorders (E.g., hypothyroidism), the space occupying lesions (e.g. brain Tumors), normal pressure hydrocephalus, or fluid Abuse. Some classes of drugs have Potential to cause cognitive impairment in older adults (For example, anticholinergics, psychotropics, analgesics, sedatives Hypnotiks)[5]. Irreversible dementias (Primary) Neurodegenerative and / or blood vessel in the brain. AD is the most common cause of irreversible dementia, 70% of all cases of dementia Primary among other types of dementia US.7 Vascular dementia (10 \ ± 20%), associated with dementia parkinson's disease, Lewy bodies dementia frontotemporal dementia[6].

TABLE I: THE DIAGNOSTIC CRITERIA FOR DEMENTIA

1. Two or more regions of the progressive decline in cognition:
a) Memory (the ability to learn and remember new information)
b) The language (speaking, reading, writing)
c) Executive function (reasoning, decision making, plan)
d) Visuo spatial function (the ability to recognize faces and objects)
e) Execute (the ability to perform purposeful movements)
f) Personality, mood or behavior changes
2. Cognitive impairments:
a) Operations (with the ability to perform activities intervention daily Life)
b) Represents a decrease from the previous level of functioning
c) Delirium or mental disorder (eg, are not due to depression)
d) Are set using the patient's history confirmed by informants (such as family members) and cognitive target evaluation.

B. Epidemiology of AD

AD is an important health, social and financial burden to society, with the United States and many other countries around the world is an important public health problem. An estimated 5 million Americans with a new diagnosis every 68 s. In the United States, Alzheimer's disease is the fifth leading cause of death among older adults and people living with dementia approximately 200,000 million dollars annually are spent on direct care. Worldwide, an estimated 35 million people suffer from AD or other dementias, and it is expected about 65 million people in 2030 (115 million people) by the madness.2050).AD is a multifactorial disease with no known single cause, and the many factors associated with the development and progress of convertible and non-convertible risk. Age is the greatest risk factor for the development of advertising. Rapidly developing AD increases with age, approximately every 5 years after age 65 is expected to double. The vast majority of people over 65 suffer from AD and late or sporadic AD (all cases 95%). Rare genetic mutations associated with the development of AD before the age of 65, "earlyonset" or "family" AD (5% of all cases) is known as. Individuals with familial forms of autosomal dominant AD, either Presenilin chromosomes 1 and 14, or amyloid precursor protein (APP) gene located on chromosome 21, in addition to changes in the genes of individuals with Down syndrome (trisomy 21) syndrome quickly increases the risk of developing Alzheimer's disease[7].

Genetics of sporadic AD is more complex and less well understood. It is known that the apolipoprotein AD (APOE) allele epsilon four located on chromosome 19 is a risk factor for the development of sporadic AD. AD prevalence is higher among women, reflecting women's longer life expectancy. Low educational level of AD dementia, the idea that a person's cognitive reserve education and to increase its resistance to AD pathology consistent with acts associated with an increased risk of. Both have a lot of evidence that the cerebrovascular risk factors play an important role in the development and progression of AD suggests; Diabetes, high blood pressure, obesity and smoking, people with a history of a substantially increased risk of advertising. AD family history in first degree relatives and a history of head trauma with loss of consciousness also are risk factors for developing AD[8].

C. Neuropathology of AD

AD is a progressive neurodegenerative brain disorder that causes disruption of the structure and is critical to normal brain function. At the cellular level, is characterized by AD. Cortical neurons, especially a progressive loss of pyramidal cells, mediated by higher cognitive functions. Evidence also suggests that early synaptic dysfunction in AD disease process causes neural circuits disrupting communication within the key to memory and other cognitive functions[9]. AD related degeneration begins in the medial temporal lobe, especially the hippocampus and entorhinal cortex. Damage to memory and learning deficits in brain structure that typically seen with AD results in early clinical manifestations. Degeneration of the temporal association cortex and parietal regions extends. As the disease progresses, the degeneration of most of the rest of the neocortex can be seen in the frontal cortex and in the end. The obvious reason is the fact that advertising Hippocampal formation and the cerebral cortex prime fibers (fornix and cingulum), amygdala, thalamus and cingulate gyrus connect several components, including the limbic system, damage[10]. Neurodegeneration the broad patterns, affecting both limbic neocortical areas, closely cognitive deficits and behavioral changes experienced by patients with AD is associated with the set. Cognitive impairment in multiple domains (memory, language, reasoning, executive and visuospatial function), in addition to AD patients and often a low mental ability to perform activities of daily living, emotional and personality disorders, showing the ability to experience [11-12].It has been theorized that the neuronal loss observed in AD is related to abnormal protein deposition in and out of neurons. The main pathological lesions of AD are known as plaques and tangles. Abnormal protein mediated neuronal pathways that memory and other cognitive functions of the ministry with stereotypic pattern are stored in the brain cortex. Senile plaques extracellular amyloid beta amyloid protein accumulation and insoluble protein (Aβ) consist. Normally, cells throughout the life of soluble Aβ released after cleavage of APP[13]. A cell surface receptor. Abnormal cleavage of APP in the dense leaves and formation of senile plaques contain beta AD resulting in the precipitation of Aβ. It is believed that microglia and astrocytes to clear the amyloid aggregates mount an inflammatory response, and the inflammation probably adjacent neurons and their neurites (axons and dendrites) that causes destruction. "Neurofibrillary tangles" (NFT) intracellular proteins which abnormally hyperphosphorylated tau microtubule protein normally acts as a stable and intracellular transport (axonal vesicular) plays a role are added. NFT, neuronal function and survival appropriate (for example, synaptic vesicles neurotransmitters, neurotrophic factors and mitochondria) due to the death of neurons in the end required components can interfere with normal axonal transport.

Sufficient evidence to consider that the formation and amyloid deposition in the cerebral cortex of 10-20 years before the onset of clinical disease in AD supports an early disease processes. Despite this, the growth of NFT formation and deposition of plaques in the time sequence of events is open to debate. In fact, a recent study shows that the initial formation NFT brainstem medial temporal lobe instead be and the first appearance of amyloid plaques in the neocortex can begin [14].

D. Diagnosis of AD

The gold standard for the diagnosis of AD an autopsy (postmortem) pathologic evaluation. The presence and distribution in the brain of plaques and NFT "fixed" AD and enfermedad.AD stage clinical scenarios used to establish the diagnosis, the diagnosis of AD is based largely on clinical history and physical neurological examinations and neuropsychological evaluation, and ancillary tests through selective exclusion of other etiologies. The clinical diagnosis of AD, compared to 70-90% accuracy of diagnosis and more precisely. In special environments such as memory disorders clinic was built [15]. The cornerstone of the consensus clinical diagnosis in 1984 and the first set of criteria established by the National Institute on Aging, last

updated in 2011. The Alzheimer's Association (NIA- AA) working group. NIA diagnostic criteria. "Potential" for the diagnosis of AD dementia AA is summarized in Table 2.

TABLE II. THE DIAGNOSTIC CRITERIA FOR PROBABLE AD DEMENTIA

1.	The presence of dementia, according to Table 1.
2.	Gradual onset of symptoms for months or years
3.	The history of progressive cognitive impairment.
4.	Initial presentation can be amnestic or amnestic.
5.	No evidence of other causes of cognitive impairment; cerebrovascular disease, or other neurological dysfunction syndrome / disease therapy.

When the patient's cognitive impairment is an abnormal clinical picture or it is suspected that other etiologies, except for AD, "possible" should the DA dementia diagnosis is recommended. Advertising on the physical and neurological examinations on patients usually have normal findings. To help with differential diagnosis, clinical features that distinguish.

TABLE III IRREVERSIBLE DEMENTIA, SOME OTHER CAUSES OF DEMENTIA WITH ABSTRACT ADVERTISING

Clinical feature	Alzhemier's dimentia	Vascular dimentia	Parkinson's dimentia	Dementia with Lewy bodies	Frontotemporal dimentia
Patient profile	≥65years old	≥45years old Vascular risk factors	≥ 65 years old	≥ 75 years old(mean)	50-70 years old 50% autosomal dominant
History	Gradual onset and deterioratio n	Acute onset step-wise deterioration	Acute onset deterioration	Acute onset deterioration	Acute onset deterioration
Initial symptoms	Memory loss	Executive dysfunction	Visual hallucination	Visual hallucination fluctuating attention	Memory intact Disinhibition ,apathy or aphasia
Physical findings	No motor impairment (until last stage)	Pyramidal (upper motor neuron) signs	Parkinsonis m (precedes ,dementia by 1 year)	Parkinsonis m (presents within,1 year of dementia)	Usually none (rarely associated with motor neuron disease)

Laboratory studies and neuroimaging diagnostic criteria only for research purposes or advertising are used as an adjunct to, especially demencia.Los unique structural brain lesions and laboratory studies rule out "reversible" to identify the causes the American Academy of neurology for the treatment of dementia as part of regular is recommended serum B12, thyroid stimulating hormone (TSH) and free thyroxine (T4) .Structural magnetic resonance imaging (MRI) or useful CT scan normal pressure hydrocephalus, brain hematomas, brain tumors and cerebrovascular lesions without contrary to rule[16].

E. Treatment of AD

There is no cure for AD, and pharmacotherapy for the disease is still in its infancy. Approved drugs for the treatment of AD likely help control the symptoms of AD, but progress is slow or reverses the course of the disease itself. Currently, the issue of AD-therapy drugs that target the brain's neurotransmitter system. E glutamate and acetylcholine neurons and their associated mainly affects synapses, and the loss of advertising first cognitive symptoms associated with the well. Acetylcholinesterase inhibitors interfere with the breakdown of acetylcholine in AD patients to help improve memory function and attention. Neurotransmitters at the synapse. Currently there are three cholinesterase inhibitors approved by the FDA: rivastigmine and galantamine (for mild to moderate AD), and Donepezil (for all stages of AD). Memantine is a drug by the FDA for use in moderate to severe AD is approved, but NMDA receptor antagonists (glutamate), a different class of drugs known as belongs to. Both classes of drugs are generally well-gastrointestinal disorders, dizziness and headache, the most common adverse effects observed, with the

bearing. In recent years, several drugs in clinical trials of disease-modifying rated ads, and many others are being tested in ongoing trials. Drugs that reduce the amount of protein in the brain acts to Aβ the most attention because it has received Aβ major pathogenic role in AD attributed to literature. Secretase inhibitors of a class of drugs, the secretase enzymes (protease) APP cleaving Ab production are disrupted. Another strategy that has been tried drugs by active or passive immunization is using to promote the elimination of Aβ .Writing of this article, the first step of many trials three different amyloid-lowering drugs has failed to demonstrate clinical efficacy. Many explanations observed with these disease modifying agents failed repeatedly in clinical trials have been proposed to explain. One possibility is that the Aβ may be a less dominant role or AD in the pathogenesis of the different role that had already been raised, of course, an issue that will remain controversial in the near future. However, other therapeutic strategies for AD, amyloid-based therapies are being tested as well, though without great clinical successes have not been reported yet. One promising avenue which abnormal tau protein drugs that target is the development of NFT[17]. Another important source of potential advertising drugs are drugs that are already on the market, such as diabetes, hypertension and infectious diseases such as non-advertising signs, are approved for the group.

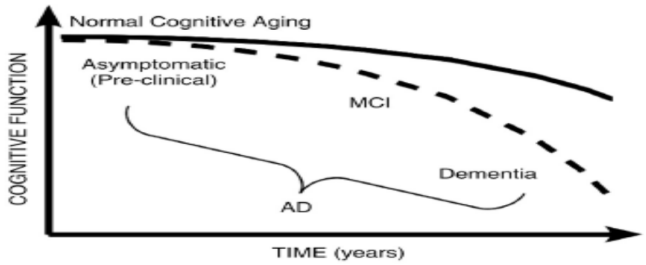

Figure 1. Alzheimer's disease (AD), a progressive development. preclinical state, mild cognitive impairment (MCI) and AD (dashed line) normal cognitive aging (solid line) is shown the relationship between the relative phase of the madness

"Reuse" or drug "repositioning 'of this strategy can greatly accelerate the discovery of new treatments DA and other neurodegenerative disorders (e.g., Parkinson's disease for use in the antiviral drug amantadine) have been used in the past for. Advertising is necessary because early diagnosis and timely therapeutic intervention before the onset of dementia disease can begin years or even decades. As such, such as individuals with MCI develop dementia who are at risk for AD, in a population of people without being given more emphasis on the conduct of clinical trials.

III. Mild Cognitive Impairment

A. The MCI Concept

MCI is a syndrome memory and / or other cognitive abnormalities associated with the normal aging process is characterized by decreased sensation over. (Fig. 1) .The most commonly used diagnostic criteria for the diagnosis of MCI MCI is often a precursor to dementia or a transitional state between healthy cognitive aging and dementia are seen as Peterson and his colleagues at the clinic May proposed (table 4). The researchers also found several subtypes of MCI depending on different neuropsychological profiles have proposed. MCI, mnemonic memory loss, while amnesiac MCI not only deficiencies in memory and other cognitive domain is involved (for example, executive / focus function, language, and visuospatial function). Multi-domain MCI is characterized by deficiencies in memory and memory functions[18].

B. Epidemiology of MCI

Large epidemiological population-based studies in both the US and Europe over 65 years is estimated that 3-24% prevalence among adults is the ICM, with a higher prevalence in older people. Prospective longitudinal studies indicate that patients with MCI progress to dementia annual rate, based on characteristic clinical fellows in the community for people with those with the highest rates show than 3-15%. In general, the rate of progression from MCI to dementia in older adults in the general population, well above the 2% annual growth rate of incidence of dementia . Among patients with MCI convert the madness, AD is the most common etiology. However, the risk of progression of MCI subtypes vary accordingly; While no amnestic MCI progress more often non-AD dementia, including vascular dementia forms, amnesic MCI and multi-domain AD progression of MCI subtypes, more often. In addition, patients with amnestic MCI than those

with a domain E are greater risk of developing a multi-domain. While many individuals with MCI develop dementia, cognitive, a large proportion will remain stable or even better, the general cognitive state (Fig. 2) returning. As a whole, epidemiological research shows that ICM is a useful concept that pre-dementia stage of AD describes, but in terms of etiology and outcome is a heterogeneous clinical syndrome.

C. Biomarkers oF AD and MCI

Neuroimaging and other biomarkers of AD and MCI are many approaches to the study being used. In the short term, ad biomarkers, improve the selection of patients in clinical trials at the start of the long-term biomarker to identify patients at high risk for treatment and the need to control the progress of disease and treatment needs for reaction. Widely used approach in this section and related biomarkers in AD and MCI is a description of some of the findings.

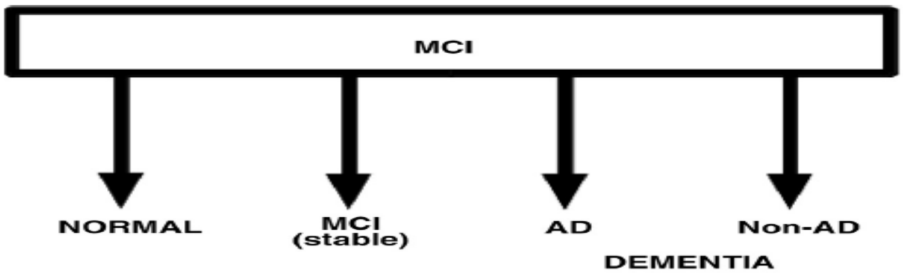

Figure 2: Mild cognitive impairment (MCI) in patients with clinical outcomes. Eventually many patients with MCI or Alzheimer's disease dementia (AD) or other reasons developed (eg, stroke) is due. However, a high proportion of patients with MCI and cognitive cognitive stable living situation back to normal

IV. Magnetic Resonance Imaging

MRI uses a strong magnetic field and radio frequency waves by non-invasively measuring the energy released by the brain structure characteristics of proton such gray matter, white matter, and cerebrospinal fluid (CSF) within as many tissue components. Big MRI in patients with MCI and AD brain atrophy has been used to study regional patterns. The medial temporal lobe, the hippocampus and entorhinal cortex in particular include atrophy, the first and most prominent feature in the ad is clear magnetic resonance and MCI progress to AD dementia predicted. Large MRI, patients with AD also show a significant increase in the lateral ventricles, the parts of which are adjacent to the medial temporal lobe.Advertising tensor imaging (DTI), a technique based on MRI. The spread of water molecules, in the white matter of the brain is able to describe the organization and quantitative researchers to assess the integrity of white matter fiber to the branches allows. DTI studies that show the ad and in the white matter of MCI disturb main routes Brain, especially those within the limbic system (such as fornix and cingulum). Finally, functional magnetic resonance imaging (fMRI) is a technique that indirectly depend on the level of brain activity, blood oxygen measuring hemodynamic function evaluates neuroimaging. A promising application of FMRI (as "resting state fMRI" is known) is a measure of the intrinsic brain activity that occurs independently of any external stimulus.FMRI studies that show the ad in the quiescent state and are associated with a lack of MCI Communication (functional connectivity) the default mode network (DMN), within the areas of the brain involved in memory and internal processing of information is a network.

TABLE IV.THE DIAGNOSTIC CRITERIA FOR MCI

1. Subjective cognitive complaint corroborated by an informant.
2. Objective memory and /or other cognitive impairments that :
(a) Are abnormal for the individuals age and education, as documented using neuropsychological testing
(b) Represents a decline from previous levels of functioning
3. Normal ability to perform activities of daily living
4. Absence of dementia

V. Positron Emission Tomography

Positron emission as a radioactive tracer 18F-fluorodeoxyglucose (FDG- PET) is a nuclear imaging technique that uses tomography measures regional cerebral metabolism. FDG- PET hypometabolism in the posterior cingulate cortex and precuneus of advertising is the first detectable signal. The hypometabolism the disease is detected in the state of MCI. FDG- PET also various forms of dementia, frontotemporal dementia, especially in contrast to distinguish advertising has proven to be of value. Based PET in vivo imaging amyloid A recent development is the development of the radioligand binds to a specific use Brain amyloid. Pittsburgh Compound B (PIB) on the basis of a targeted carbon amyloid 11 ligand is widely used in research environment. Advertising patients Show brain, which indicates a wide distribution of cortical amyloid deposition temporal, parietal and frontal areas of GDP increased bond. FDA-approved labeling a ligand different amyloid, fluorbetapir fluorine -18, 2012.PET Amyloid-based image in a new and exciting diagnostic tool for clinical use is a major molecular lesions noninvasively detects EA, but still many practical concerns about its use in clinical settings are. In addition to its high cost, there is a positive amyloid scan is a concern about the clinical utility. amyloid negative analysis seems Ruled that a patient's cognitive impairment E (high negative predictive value) is due to a positive amyloid scan may be positive because it is much less informative .Cognitively normal older adults and other neurological conditions many ads (positive predictive value) in people with. For now, amyloid-based PET images in advertising routine clinical use for patients with Medicaid or are not covered by Medicare, but only for limited use (for example, rule out the EA or patients in clinical trials for the selection of the).

VI. Fluid Biomarkers

Also for the diagnosis of AD based protein biomarkers in CSF and blood plasma are investigated. (P-tau in the CSF, many studies have used different immunoassays for measuring protein levels, patients find that ad isoform 42 amino acid peptide decreased AB (now 42) and phosphorylated tau levels high show) .In 2007 e option plasma biomarkers for early detection has been proposed as a promising CSF biomarkers. A recent longitudinal study showed that basal Ab-42 / P-tau ratio can predict the progression of MCI to AD. Years, other studies of immune cell signaling, metabolism is examined clinical utility, and diseases related to plasma proteins, but findings have been inconsistent. In general, more work needs to be done to standardize measurement CSF and plasma proteins and determine the clinical utility of biomarkers the diagnosis of AD.

VII. Conclusion

For more than a century since Alois Alzheimer first described in terms of advertising, this disease has made great strides in understanding the biological and clinical aspects. As they MCI, advertising made great progress in the pre-dementia phase characterization, and diagnosis and treatment options available for managing e has improved. Our EA to "cure" the ability to know the cellular and molecular processes that eventually go wrong, not only depends on having an accurate picture, but also to enable early diagnosis and timely therapeutic intervention is optimal biomarkers of risk in individuals. E for early detection of clinically useful neuroimaging and other biomarkers in recognition of the urgent need to develop the NIA Alzheimer's Disease Neuroimaging Initiative (ADNI) ongoing since 2004 sponsored ADNI, which is similar to the Framingham Heart Study in your ambition , one of the largest projects of its kind public-private partnership and wants to collect longitudinal neuroimaging data MCI biological samples (such as blood and CSF), AD and healthy older subjects, clinical, and neuropsychological assessment as well. It ADNI initiative and other similar mass madness and quickly advance our knowledge about advertising and advertising that stimulates the development of effective treatments existing today much more likely. To conclude, the reader, some key issues that must be solved in the future, as we in the 21st century advertising a "cure" is to move towards the left with:

(1) (A) AD is the optimal combination of biomarkers for early detection; And (b) to monitor disease progression and response to therapy?

(2) Whether (a) the optimal therapeutic strategy for the prevention of AD; B) Treatment of advertising; And (c) vs. familiar sporadic advertising? (i.e., therapeutic objectives, the lifestyle, the optimal time to intervene against the amendment role of drugs),

(3) the potential benefits and changing therapeutic strategy (what are the harms associated with one) that open with dementia treatment consisted of a) where we treat people with MCI and finally, (c) where we have

a people who are asymptomatic but a biochemical treatment patterns and / or show images of biomarkers similar to AD? We compared patients for the treatment of abnormal lab results get closer? For example, we will meet To pledge an asymptomatic individual treatment showed a pattern similar to the DA for biomarkers such as due to its high resistance to deformation of cognitive reserve "First, do no harm," but does not intend to develop cognitive impairment (AD).

REFERENCES

[1] Alzheimer's Association, "2015 Alzheimer's disease facts and figures," Alzheimers Dement, vol. 11, no. 3, pp. 332–384, 2015.

[2] R. L. Buckner, A. Z. Snyder, A. L. Sanders, M. E. Raichle, and J. C. Morri, "Functional brain imaging of young, nondemented, and demented older adults," J Cogn Neurosci, vol. 12, pp. 24–34, 2000.

[3] B. Jin, A. Strasburger, S. J. Laken, F. A. Kozel, K. A. Johnson, M. S. George, and X. Lu, "Feature selection for fMRI-based deception detection," BMC Bioinform, vol. 10, no. S15, 2009.

[4] H. Melero, A. Pe˜na-Meli´an, M. R´ıos-Lago, G. Pajares, J. A. Hern´andez- Tamames, and J. Alvarez-Linera, "Grapheme-color synesthetes show peculiarities in their emotional brain: cortical and subcortical evidence from VBM analysis of 3D-T1 and DTI data," Exp Brain Res, vol. 227, no. 3, pp. 343–353, 2013.

[5] S. Bray, C. Chang, and F. Hoeft, "Applications of multivariate pattern classification analyses in developmental neuroimaging of healthy and clinical populations," Front Hum Neurosci, vol. 3, no. 32, 2009.

[6] S. Kl¨oppel, C. M. Stonnington, C. Chu, B. Draganski, R. I. Scahill, J. D. Rohrer, N. C. Fox, C. R. J. Jack, J. Ashburner, and R. S. Frackowiak, "Automatic classification of MR scans in Alzheimer's disease," Brain, vol. 131, pp. 681–689, 2008.

[7] E. E. Tripoliti, D. I. Fotiadis, M. Argyropoulou, and G. Manis, "A six stage approach for the diagnosis of the Alzheimer's disease based on fMRI data," J Biomed Inform, vol. 43, pp. 307–320, 2010.

[8] R. Arma˜nanzas, Consensus Policies to Solve Bioinformatic Problems.LAP LAMBERT Academic Publishing, 2012.

[9] W. Penny, K. Friston, J. Ashburner, S. Kiebel, and T. Nichols, Eds., Statistical Parametric Mapping: The Analysis of Functional Brain Images. Academic Press, 2006.

[10] A. C. Evans, D. L. Collins, S. R. Mills, E. D. Brown, R. L. Kelly, and T. M. Peters, "3D statistical neuroanatomical models from 305 MRI volumes," in Proc IEEE-Nuclear Science Symposium and Medical Imaging Conference, 1993, pp. 1813–1817.

[11] G. Flandin and K. J. Friston, "Statistical parametric mapping," Scholarpedia, vol. 3, no. 4, p. 6232, 2008.

[12] L. I. Kuncheva and J. J. Rodr´ıguez, "Classifier ensembles for Fmri data analysis: An experiment," Magn Reson Imaging, vol. 28, no. 4, pp. 583–593, 2010.

[13] J. C. Platt, "Fast training of support vector machines using sequential minimal optimization," in Advances in Kernel Methods, B. Sch¨olkopf, C. J. C. Burges, and A. J. Smola, Eds. MIT Press, 1999, pp. 185–208.

[14] R. E. Fan, K. W. Chang, C. J. Hsieh, X. R. Wang, and C. J. Lin, "Liblinear: A library for large linear classification," J Mach Learn Res, vol. 9, pp. 1871–1874, 2008.

[15] H. J. George and P. Langley, "Estimating continuous distributions in bayesian classifiers," in Proc of the Eleventh Conference on Uncertainty in Artificial Intelligence. Morgan Kaufmann, 1995, pp. 338–345.

[16] L. Breiman, "Random forests," Mach Learn, vol. 45, pp. 5–32, 2001.

[17] T. K. Ho, "The random subspace method for constructing decision forests," IEEE Trans Pattern Anal Mach Intell, vol. 20, no. 8, pp. 832– 844, 1998.

[18] L. I. Kuncheva and J. J. Rodr´ıguez, "Classifier ensembles with a random linear oracle," IEEE Trans Knowl Data Eng, vol. 19, no. 4, pp. 500–508, 2007.