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NEUROPHYSIOLOGY AND PATHOLOGY IN DEMENTIA AND ALZHEIMER'S DISEASE

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ABTRACT

Madness is a set of symptoms that arise in the brain and is associated with literacy, memory, thinking, communication, language, and poor judgment. Alzheimer's complaint and vascular madness are the two most common types of madness. It isn't a specific complaint, but several conditions can beget madness. Madness is generally a habitual or patient pattern in which there's good internal functioning (i.e., the capability to reuse study) beyond what can be anticipated from normal aging. It affects memory, thinking, shape, appreciation, counting, reading capability, language and judgment. Mindfulness isn't affected. Impaired internal function is frequently associated with, and is occasionally anteceded by a drop in emotional control, social geste, or provocation. Madness is associated with neurodegenerative complaint, and a set of symptoms that develop in the brain is caused by neurological dysfunction and brain cell death. Madness occurs when the brain is affected by a complaint that causes madness. Treatment for madness is generally grounded on the history of cases with psychiatric symptoms and neuroimaging. Alzheimer's complaint (Announcement) is a complaint that causes the degeneration of brain cells and is the leading cause of madness, characterized by a drop in thinking and independence in diurnal particular conditioning. Announcement is considered a multifactorial complaint two main suppositions have been proposed as the cause of Announcement, the cholinergic thesis and the amyloid thesis. In addition, colorful threat factors, similar as advanced age, inheritable factors, head injuries, vascular conditions, infections, and environmental factors, impact the complaint. It's the most common cause of madness in people aged 65 and over. This review deals with the study of the physiology and pathophysiology of madness and Alzheimer's complaint.

KEYWORDS: Dementia, symptoms, causes, physiology, pathology, neurophysiology, alzheimer disease.

DEMENTIA

Madness may be a set of symptoms that arise within the brain and is related to literacy, memory, thinking, communication, language, and poor judgment. Alzheimer's complaint and vascular madness are the 2 commonest feathers of madness. It's not a named complaint, but several conditions can beget madness. Madness is generally a habitual or patient pattern during which there is good internal functioning (i.e. the power to reuse study) beyond what are frequently anticipated from normal aging. It affects memory, thinking, shape, appreciation, counting, reading capability, language and judgment. Mindfulness is not affected. Deterioration of internal function is generally related to and occasionally anteceded by a decline in emotional control, social geste or provocation (WHO, 2017).

Madness is related to neurodegenerative complaint, and a group of symptoms that develop within the brain is caused by neurological dysfunction and whim-whams cell death. Clinically, this complaint are frequently defined as a pattern that causes a drop in cognitive impairment (i.e. attention, memory, communication, language, visuospatial chops, operation function) (Pond. D, et.al, 2012). Predicting madness within the early stages could also be important to enhance treatment before brain injury. Beforehand opinion of madness is rested on symptoms. Significant progress has been made in recent times to spot the primary stages of madness using biomarkers. These advancements include biochemical, neuroimaging, inheritable and neurophysiological biomarkers (Cedazo Minguezet.al, 2010, Hampelet.al, 2010). Madness occurs when the brain is suffering from certain diseases that beget deceleration (Borson. S et. Al, 2013). Treatment for madness is generally dependent; Clinical history of cases with neurological and neuroimaging psychiatric symptoms. (Hampel. H, et.al, 2010).

Worldwide prevalence of dementia

The number of individualities living with madness worldwide reached 47.47 million in 2015, 75.63 million by 2030 and 135.46 million by 2050 (Alzheimer complaint transnational 2013). The frequence of madness is growing fleetly from 2-3 among people aged 70 to 75 to 20-25 among people aged 85 or aged (Ferri et. Al

2005). Especially for women who are important aged than men, it's anticipated that there will be an increased threat of Alzheimer's age- related changes (RR = 1.3). Thus, vascular madness and other cardiovascular and atherosclerotic conditions are more common in men. Analysis of aggregated data from a European population study suggests that the average frequence of age is6.4 for madness and4.4 for Announcement in the senior (over 65) (LoboA., etal. 2000). In the USA, a 9.7 Announcement frequence was attained on the base of a sample study representing a country over the age of 70 people (PlassmanBL., et al 2007). Encyclopedically, the frequence of madness worldwide is estimated at3.9. for people over the age of 60 with indigenous frequence of1.6 in Africa,4.0 in China and the West Pacific regions,4.6 in Latin America,5.4 in Western Europe and 6.4 in North America (FerriCP., Et 2005). According to coffers, further than 25 million people worldwide suffer from madness, the maturity of people suffering from Alzheimer's complaint (FerriCP., En al 2005, Wimo A, et al 2003, Brookmeyer R, et al, 2007). The number of individualities with madness is prognosticated to double every 20 times. Despite the different addition procedures, colorful meta-analyzes and public tests showed nearly the same frequence of Announcement in all regions (LoboA., etal. 2000, Plassman BL et al, 2007, Dong MJ etal., 2007, Scazufca M et al. Al, 2008).

Alzheimer's Disease

Alzheimer's disease (AD) is the most common form of dementia, and 62% of all people with dementia have AD. Vascular dementia accounts for 17% of people with dementia and 10% of people have symptoms of Alzheimer's and vascular dementia; This is known as bipolar disorder. Figure 3 shows the occurrence of different types of dementia. Alzheimer's disease is a neurodegenerative disease characterized by mental and memory impairment, progressive impairment of daily activities and various behavioral and mental disorders (Ferri et al., 2005). The main causes of Alzheimer's disease appear to be (a) reduced cholinergic activity (b) oxidative stress (c) deposition of beta-amyloid peptides in the brain. Acetylcholinesterase (AchE) plays an important role in regulating the cholinergic system, and thus inhibiting cholinesterase has become one of the most promising treatments for Alzheimer's disease. One of the main therapies is to block acetylcholinesterase and thus increase the level of acetylcholine in the brain (Lu. Et.al., 2011). It has also been suggested that inequalities between the generation of free radicals and antioxidants are the cause of Alzheimer's disease (Guglielmotto et al., 2019).

At present, 50 million people suffer from Alzheimer's disease or AD-related dementia (C., P., 2018). Several neuropathological changes in Alzheimer's disease include loss of neuronal cells, development of neurofibrillary tangles and amyloid plaque in the hippocampus, entorhinal cortex, neocortex and other brain regions (Coyle JT et al., 1983, Terry AV et al., 200). As the most common form of dementia, Alzheimer's is becoming a major global health problem for the elderly. According to current statistics (2019), approximately 50 million people suffer from A related or AD-related dementia (CP World Alzheimerâ€™s Report 2018).

Symptoms

The various clinical symptoms of Alzheimer's disease include progressive memory impairment, poor functional management, and difficulty performing normal daily activities. Early symptoms of Alzheimer's disease include changes in unconscious thinking or behavior, impaired memory about new information, and dysfunctional changes in speech and language (Tarawneh R, et.al, 2012). A patient in advanced stages of Alzheimer's disease suffers from severe memory loss, hallucinations, confusion and inability to cope and eventually dies from respiratory illness (Kalia M, et.al, 2003). Major pathological features of AD include beta A plaques, neurofibrillary tangles (NFT), gliosis, and neuronal loss (Terry RD, et.al, 1991, Iqbal K, et.al, 2016, Itagaki S, et al, 1989, Iqbal K, et al, 2002, Petrella C, et al, 2019) associated with cerebrovascular amyloidosis, inflammation and major synaptic changes (Katsumoto A, et al, 2018, Dansokho C, et al 2018, Tonnies E, et al 2017).

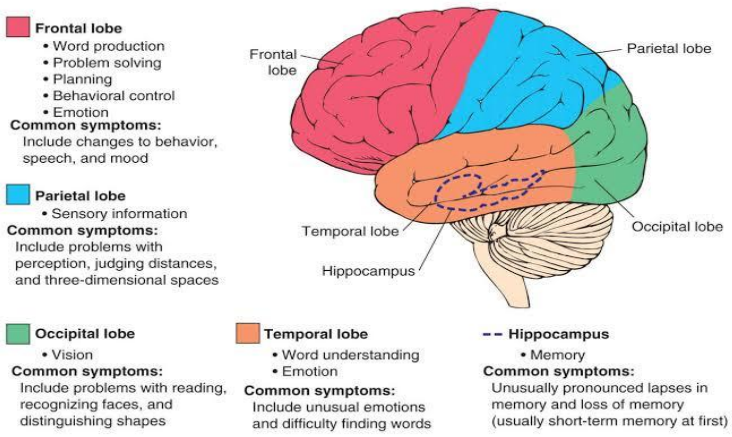

Figure 1: Symptoms occurs in different parts of brain.

Table 1: Common symptoms experienced by people with dementia syndrome.
(World Alzheimer's Report 2009; Jotheeswaran et al., 2010)

Early Stage	Middle Stage	Late Stage
The early stage is often overlooked. Relatives and friends (and sometimes professionals as well) see it as "old age", just a normal part of ageing process. Because the onset of the disease is gradual, it is difficult to be sure exactly when it begins. i) Become forgetful, especially regarding things that just happened. ii) May have some difficulty with communication, such as difficulty in finding words. iii) Become lost in familiar places. iv) Lose track of the time, including time of day, month, year, season. v) Have difficulty making decisions and handling personal finances. vi) Have difficulty carrying out complex household tasks. vii) Mood and behaviour: a) may become less active and motivated and lose interest in activities and hobbies. b) may show mood changes, including depression or anxiety. c) may react unusually angrily or aggressively on occasion.	As the disease progresses, limitations become clearer and more restricting. i)Become very forgetful, especially of recent events and people's names. ii)Have difficulty comprehending time, date, place and events; may become lost at home as well as in the community. iii) Have increasing difficulty with communication (speech and comprehension). iv) Need help with personal care (i.e. toileting, washing, dressing). v) Unable to successfully prepare food, cook, clean or shop. vi) Unable to live alone safely without considerable support. vii) Behaviour changes may include wandering, repeated questioning, calling out, clinging, disturbed sleeping, hallucinations (seeing or hearing things which are not there). viii) May display inappropriate behaviour in the home or in the community (e.g. disinhibition, aggression).	The last stage is one of nearly total dependence and inactivity. Memory disturbances are very serious and the physical side of the disease becomes more obvious. i) Usually unaware of time and place. ii) Have difficulty understanding what is happening around them. iii) Unable to recognize relatives, friends and familiar objects. iv) Unable to eat without assistance, may have difficulty in swallowing. v) Increasing need for assisted self-care (bathing and toileting). vi) May have bladder and bowel incontinence. vii) Change in mobility, may be unable to walk or be confined to a wheel chair or bed. viii) Behaviour changes, may escalate and include aggression towards carer, non verbal agitation (kicking, hitting, screaming or moaning). ix) Unable to find his or her way around in the home.

Common Causes of Dementia and Associated Characteristics
(Alzheimer's Association, 2021)
There are various common causes and associated characteristics discussed below;

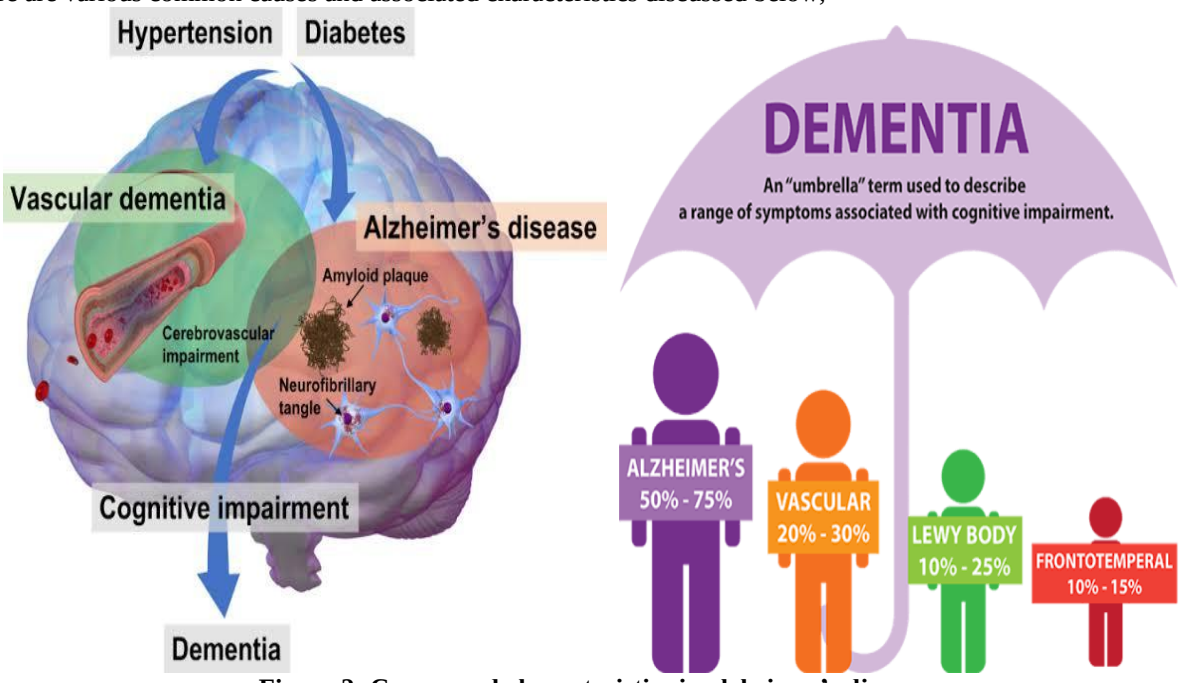

Figure 2: Causes and characteristics in alzheimer's disease.

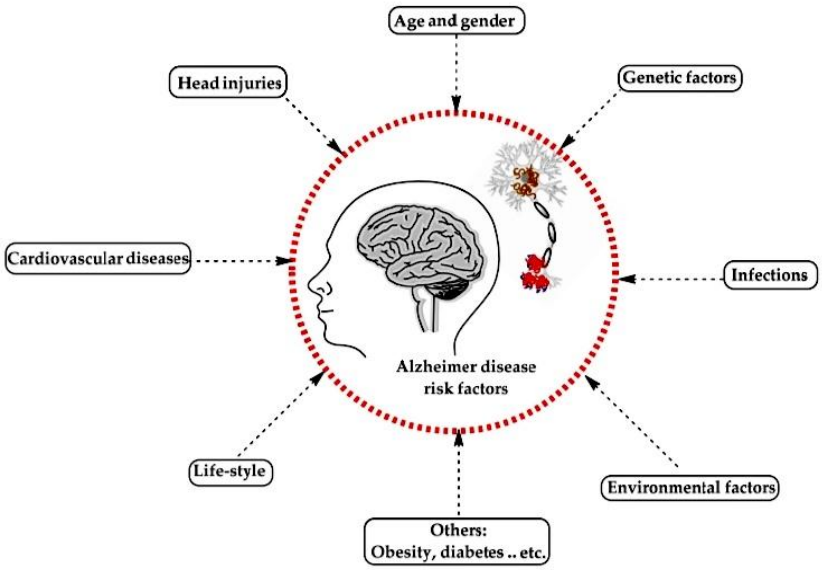

Figure 3: The risk factors for Alzheimer's disease.

Types of Alzheimer's Disease

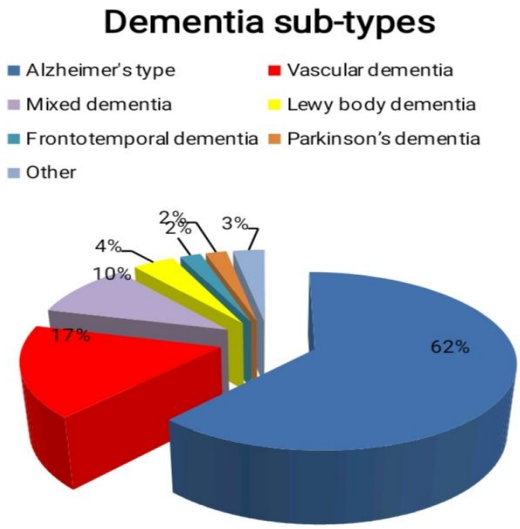

Figure 4: Dementia subtypes.

i) Vascular Dementia: It's believed to be the alternate most common cause of madness. It's more common in men. The brain needs a good blood force to supply it with sugar and oxygen. An interruption in blood force or a period of poor blood force can beget a brain injury leading to madness.

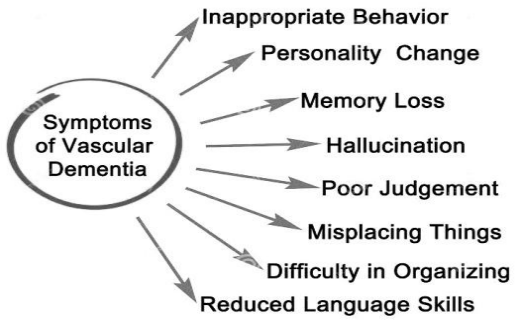

Figure 5: Symptoms of vascular dementia.

ii) Subcortical Dementia: Iit's believed to be the most common type of vascular madness. It's caused by conditions of the small deep blood vessels in the brain. These small vessels develop thick walls and come stiff and crooked, which suggests that the blood inflow through them is reduced. Small vessel complaint frequently damages the packets of whim-whams filaments that carry signals round the brain, appertained to as the substantia alba. It can also beget small areas of damage, heart attacks near the base of the brain. Small vessel complaint develops important deeper in the brain than stroke damage (Shaik and Varma, 2012).

iii) Stroke-related Dementia: A stroke occurs when the blood force to a specific area of the brain suddenly stops. In numerous cases, the blood vessels in the brain are narrowed and blocked. In some cases, seizures do as a result of a ruptured blood vessel in the brain. The size of the stroke varies depending on the position of the blocked vessel and the size of the stroke. Dislocation of blood force reduces oxygen force and leads to the death of brain towel. About 20 of people with a stroke experience madness during the first six months of a stroke (Alzheimerâ€™s Society, 2014). Multiple infarcted madness is caused by small strokes. A stroke can be so mild that bone doesn't indeed know it. Occasionally a person has a series of small strokes, known as temporal ischemic attacks. These multiple cells beget small brain cells to die and are known as heart attacks. A series of mild heart attacks can affect in increased brain damage. Depression is frequently caused by dropped blood force; This may be due to a heart attack or a period of low blood pressure (Jolley, 2009). Brian's reviews show areas of brain death caused by stroke. Inheritable revision of notch on chromosome 19-CADASIL is allowed to be one of the most common causes of vascular madness. Treatment of arterial complaint and high blood pressure can help or reduce the frequence of multiple strokes (Roman, 1999).

iv) Mixed Dementia: Mixed madness is a combination of types of madness. The most common are Alzheimer's complaint and vascular madness. A person has both types of conditions and symptoms of both conditions. People may also have Alzheimer's complaint and Lewy's complaint, which is less common (Alzheimer's Society, 2018).

v) Dementia with Lewy body disease (DLB): Lewy bodies were diagnosed by Drs. Lewy in 1912. Small circular deposits of proteins found in nerve cells. They disrupt normal brain function by disrupting the activity of chemical agents, including acetylcholine and dopamine (Alzheimerâ€™s Society, 2019b). DLB usually affects the parts of the brain that control body movement and the processing of sensory information. People with Lewy's disease often become very drowsy and have hallucinations. They may also have a rapid change in their ability to function properly, suddenly feeling confused or confused. People with Lewy's disease often fall (Jolley, 2009). Early onset of dementia, episodes of depression, hallucinations, and poor quality of life are highly marked in Lewy body disease (Ballard et al., 1999). Lewy's carcasses are also found in the brains of people with Parkinson's disease (PD). Some people with Parkinson's disease develop dementia exactly like Lewy's dementia (de Lau et al, 2005).

vi) Frontotemporal Dementia: Frontotemporal dementia is rare. It is sometimes called Pick's disease or dementia of the frontal lobe. It usually occurs in middle age. The term "frontotemporal" refers to the parts of the brain that are damaged in this type of dementia. The frontal lobe of the brain controls behavior, problem-solving, planning, and emotional control. The area of the front left lobe, for those who use the right hand, controls speech. The temporary lobes on each side of the brain have different functions. The left-handed word is usually interested in the meaning of words and object names. The right temporary lobe is often involved in facial recognition and normal objects. The human condition, social behavior, and language skills change as a result of the deterioration of the frontal and temporal parts of the brain. One does not know its severity (Alzheimer's Society, 2019c).

PAPATHOPHYSIOLOGY OF ALZHEIMER'S DISEASE

Alzheimer's disease is a progressive disease, as neurons are damaged and lost throughout the brain, especially in the cortex and hippocampus (Nussbaum, R.L et al. 2003). Changes in the function of neuronal systems that release serotonin, glutamate, noradrenaline are major physiological changes that occur in Alzheimer's disease (Wenk, G.L, 2003). Many amyloid plaques are insoluble masses of many amyloid proteins that are grouped together between neurons in the brain (Meadowcroft, MD, et al. 2009). They are extracellular and are found mainly in adults (Nelson, P.T et al, 2012). The main changes the brain undergoes are multiple amyloid plaques and neurofibrillary tangles. Amyloid plaques alone are not a sufficient substrate for advanced clinical depression in AD, but neurofibrillar (tau) disease appears to have a strong association between AD genes and the formation of multiple amyloid plaques (Nelson, PT, et al., 2012).

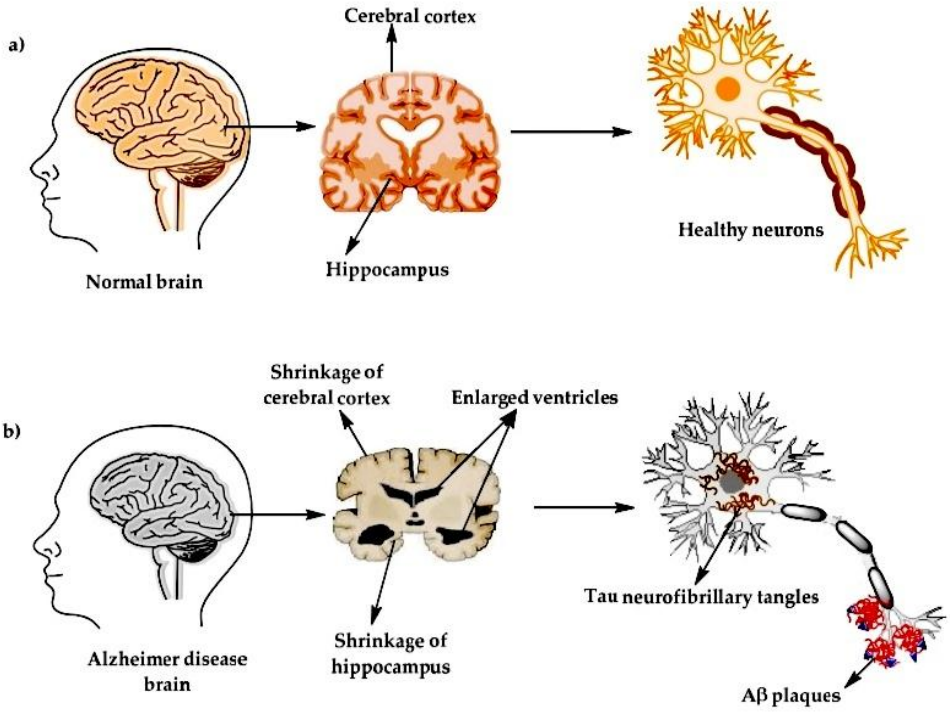

Figure 6: The physiological structure of the brain and neurons in (a) healthy brain and (b) Alzheimer's disease (AD) brain.

MECHANISM

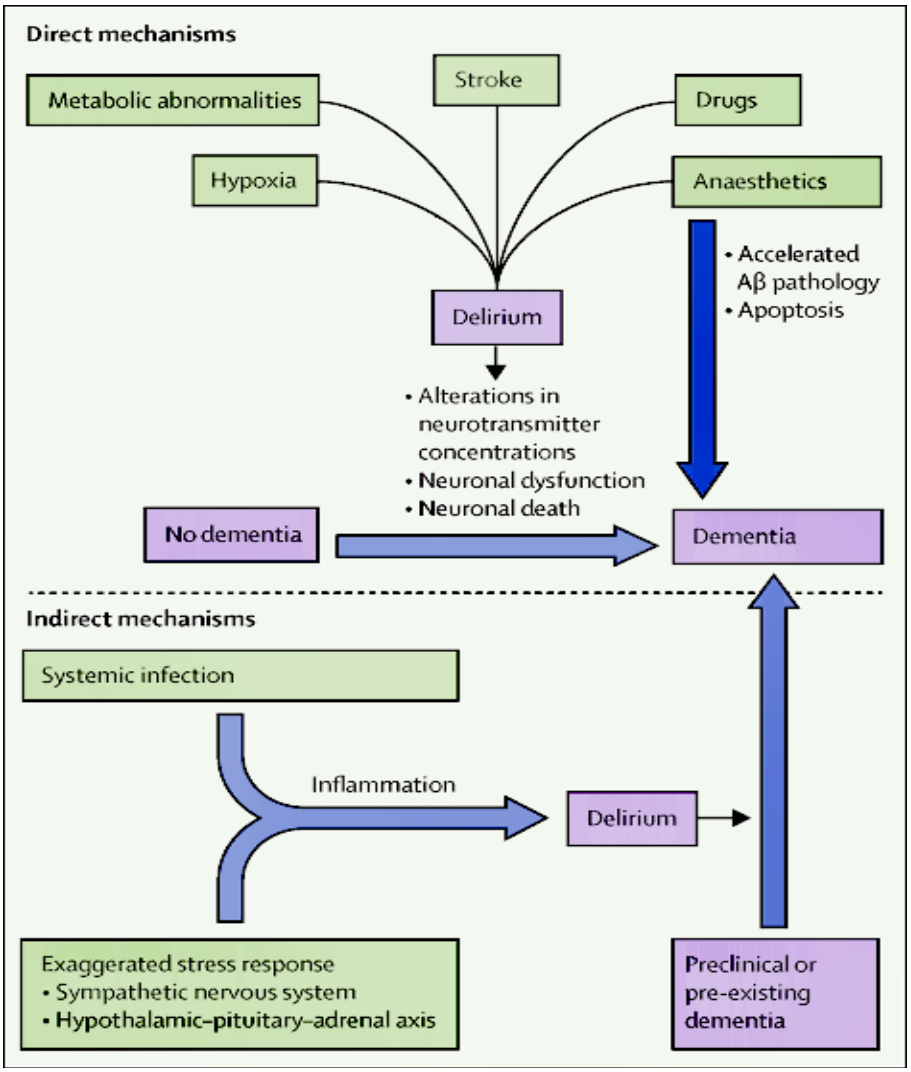

Figure 7: Direct and indirect mechanism in alzheimer's disease.

How does Alzheimer's disease present?

Loss of memory is everything and is the first sign in many cases. The gradual onset of memory loss means that (understandably) it can be attributed to normal aging and is often recognized only when considered backwards as the onset of Alzheimerâ€™s disease. The onset is mild, with severe memory loss and difficulty finding words, common symptoms in everyday life to varying degrees. Only when symptoms seriously interfere with social work and work, or are they seen by others, who feel they are continuing, where suspicion of dementia is justified. Emotional changes are common, severe depression occurs in 24-32% of cases, anxiety in 17-27%, negligence up to 41%, and delusion in 23% (Leroi et al., 2005).

Table 2: Different Levels in Alzehimers Disease (Alistair et al., 2009).

Levels in Alzehimers Disease	Observations
Mild cognitive impairment	Complaints of memory loss, intact activities of daily living, no evidence of Alzheimer's disease
Mild Alzheimer's disease	Forgetfulness, short term memory loss, repetitive questions, hobbies, interests lost, impaired activities of daily living.
Moderate Alzheimer's disease	Progression of cognitive deficits, dysexecutive syndrome, further impaired activities of daily living, transitions in care, emergence of behavioural and psychological symptoms of dementia.
Severe Alzheimer's disease	Agitation, altered sleep patterns, assistance required in dressing, feeding, bathing, established behavioural and psychological symptoms of dementia.
Very Severe Alzheimer's disease	Bed bound, no speech, incontinent, basic psychomotor skills lost.

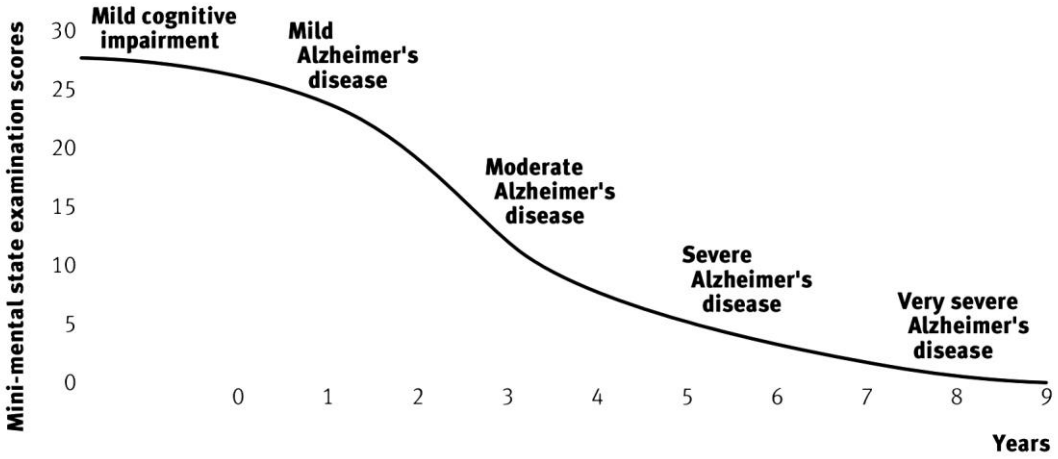

Figure 8: Graph represents different levels in Alzehimer's disease.

NEUROPHYSIOLOGY IN DEMENTIA AND ALZHEIMER'S DISEASE

There are two types of neuropathological changes in Announcement that give substantiation of complaint progression and symptoms and include (1) nasty lesions (due to accumulation), characterized by the accumulation of neurofibrillary befuddlements, amyloid pillars, dystrophic neurites, fibers neuropil and other deposits. plant in the smarts of Announcement cases. In addition (2) nasty lesions (due to leakage), which are characterized be severe atrophy due to neural, neuropic and synaptic losses. In addition, other factors can beget neurodegeneration similar as neuroinflammation, oxidative stress, and damage to cholinergic neurons.

i) Senile Plaques (SP): Senile pillars are deposits outside of beta-amyloid protein (AÎ²) cells that have a variety of morphological types, including neuritic, verbose, thick- core or old compact pillars. Proteolytic fractionalization enzymes similar as Î²-secretase and Î³-secretase are responsible for the biosynthesis of AÎ² deposits of transmembrane amyloid precursor protein (APP) (19-21). These enzymes break down APP into several amino acid fractions 43, 45, 46, 48, 49 and 51 amino acids, reaching the final forms AÎ²40 and AÎ²42. There are several types of AÎ² monomers, which include large, undoable amyloid fibrils that can form amyloid shrine and answerable oligomers that can spread throughout the brain. AÎ² plays an important part in neurotoxicity and neuronal function, so the accumulation of thick pillars in the hippocampus, amygdala and cerebral cortex can beget astrocyte and microglia stimulation, damage to axons, dendrites and loss of synapses, in addition to cognitive impairment.

ii) Neurofibrillary Tangles (NFTs): NFT is a rare component of hyperphosphorylated tau protein that in some cases can be twisted to form a helical filament (PHF) that binds and accumulates in the neuralperikaryal cytoplasm, axons, and dendrites, resulting in loss. Cytoskeletal microtubules and tubulin-related proteins. Hyperphosphorylated tau protein is a major component of NFTs in AD patients, and its evolution may indicate morphological phases of the NFTs, including: (1) the pre-tangle phase, single-type NFT, in which the protein phosphorylated tau collected there. somatodendritic compartment without PHF formation, (2) mature NFTs, characterized by fusion of tau protein filament by nucleus displacement in the surrounding soma and (3) external tangles, or NFTs phase which is a ghost, resulting in neuronal loss due to the large amount of filamentous tau protein that is partially resistant to proteolysis.

iii) Synaptic Loss: Synaptic damage to the neocortex and limbic system causes memory impairment and is usually seen early in AD. Synaptic loss mechanisms include impairment in axonal transport, mitochondrial damage, oxidative stress, and other processes that may affect subunits such as AÎ² and tau accumulation at synaptic sites. These processes eventually lead to loss of dendritic spines, pre-synaptic terminals, and axonal dystrophy. Synaptic proteins act as biomarker signals to detect synapses loss, as well as robustness, such as neurogranin, postsynaptic neuronal protein, visinin-like protein-1 (VILIP-1), and synaptotagmin-1 (Zeinab et al., 2020).

CONCLUSION

People with dementia are usually older people and most older people have a certain number of age-related health conditions. A person with dementia will have difficulty managing their health and as dementia progresses they will have difficulty managing daily activities. People with dementia will sometimes need help from hospital staff, social services and social care. It is important that caregivers have a good understanding of the types of dementia, how to diagnose it and what treatments are available. The next part of this series will focus on the diagnosis and treatment of Alzheimer's disease. The multifactorial characteristic of AD's pathogenic mechanism hinders the development of fully functional drugs for its treatment. Therefore, several researchers are continuing to search for young drug addicts in order to find treatment for AD. However, all of the drugs available so far only work on symptoms which means

that these treatments are generally unsatisfactory due to the permanent recovery of the disease after diagnosis. In addition, the maintenance of treatment from the patient himself or the caregiver is often difficult, as this type of disease often requires a combination of drugs to achieve better clinical outcomes. It is in this aspect that early diagnosis helps to preserve the memory and cognitive functions of these patients.

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