Basics of Mental Health and Clinical Psychiatry
Professor Sumit Kumar
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Lecture 24
Neurocognitive Disorders 1

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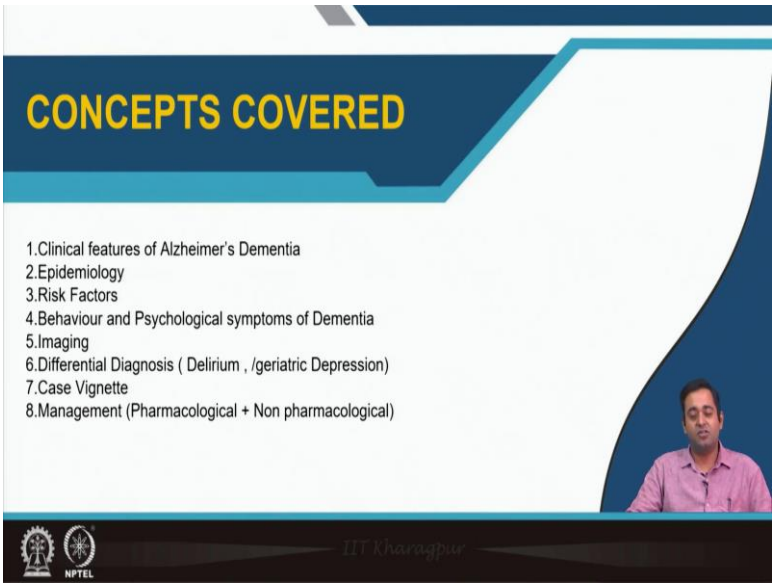

Hello everyone. Let us begin lecture number 24 neurocognitive disorders. So, topics we will be discussing is clinical features of Alzheimer's dementia, epidemiology. So, this its risk factors, behavioral and psychological symptoms of dementia imaging, the differential diagnosis that is delirium and geriatric depression. With the help of three case vignettes, we will be discussing also and lastly, the management pharmacological and non-pharmacological management.

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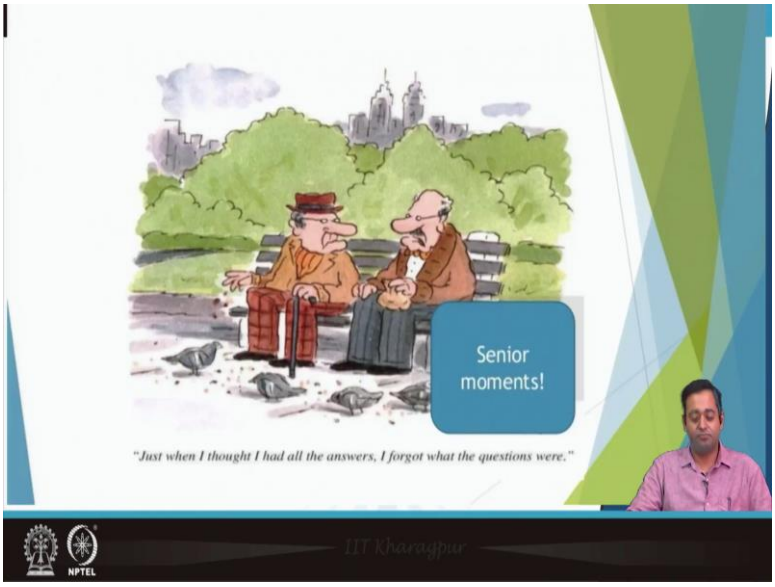

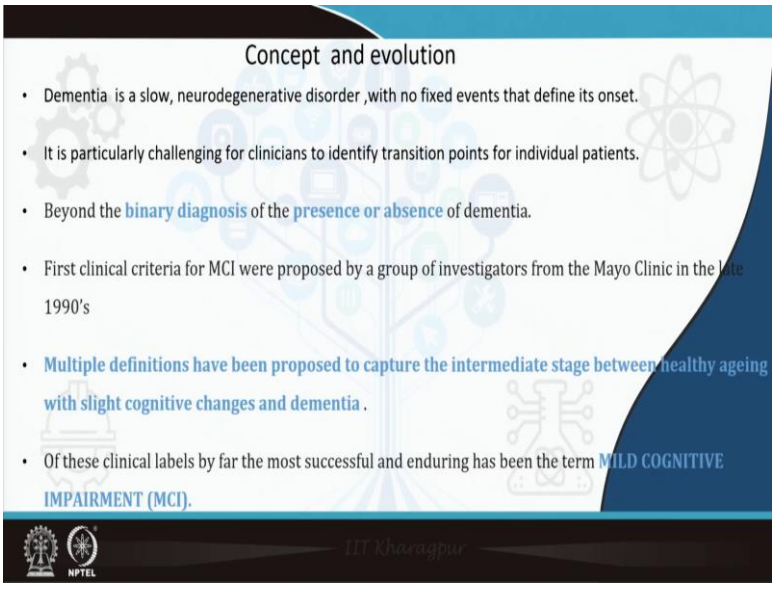

So, we all have that one family member, that we have been seeing it that they are suffering from those old age-related problems. And this old age brings a lot of problems to the life of the person who is like more or less more than 65 to 70 years old, there are medical problems associated there are orthopedic issues in medical problems, you have cardiac related issues, you have kidney problems, at times yes, you have behavioral problems and psychological issues also, which actually makes life crippled.

So, we have that one member of our members who are in that early stage and we can actually have a relatable experiences and we can actually relate his or her suffering from the literature also various textbooks and materials.

So, most important psychiatric illness which the age of more than 65 years they manifest with is dementia. So, what is a dementia? Dementia is actually a slowly and progressive neurodegenerative disorder with no fixed events that defines its onset. So, we actually do not know from which stage for which stage of the illness of the illness starts from what age so there is no predefined age criteria given, so that we can actually diagnose the disease.

So, that becomes a challenge for the clinicians to actually have a transitory point, this is the position this is the time zone, this is the condition this is the situation from where the patient can have, can manifest with the symptoms which can later progresses and developed into dementia.

So, the problem of binary diagnosis that is presence and absence of dementia was actually encountered previously, where you do not have that transitory phase is to document this is the phase this is a situation from here on the patients might have a propensity to develop the dementia. So, in early 1990s, the researchers the group involved they from Mayo group they went on to develop an entity called mild cognitive impairment.

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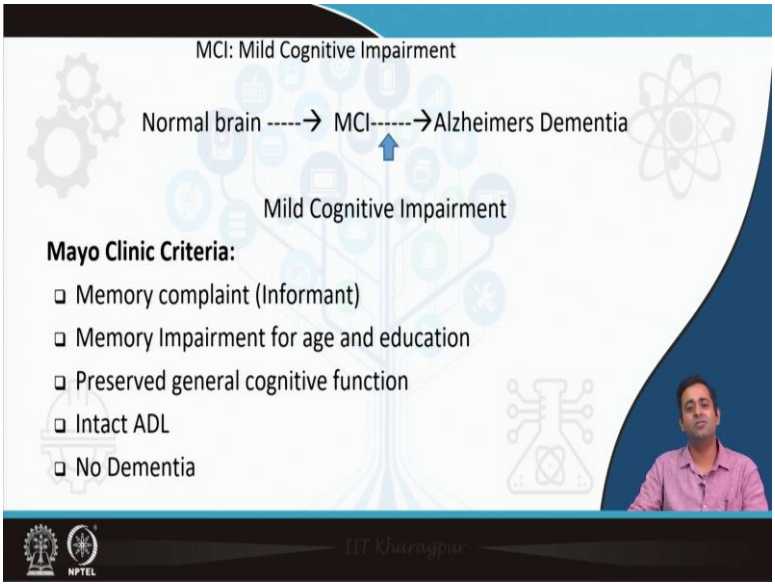

So, what is this mild cognitive impairment, it actually became the transitory points from a normal brain to dementic brain. So, this MCI model mild cognitive impairment, in which the patient develops some features some symptoms, which later on progresses to or went on to develop a dementia, what are those features, these are subjective complaints of memory. Then, this memory complaints can be elaborated by the caregivers of like of the patient, those who are actually taking care of the patient, the informant, with preserve general cognitive function.

Now, cognitive function means all those areas of memory executive functions, how you act, how you exercise, how you move your hands, how you coordinate your movements, how you talk to your people, your family members, friends, everything.

So, that is preserved, you are not having problems in those areas, there is intact ADL, ADL means activity of daily living your necessary day to day life activities. You wake up in the morning, you brush your teeth, you go for toilet, you take you do bathing, you go for your work, you come back in the evening have meals so all those things is being coordinated your activity of daily living is preserved and there is no dementia. So, this is how mild cognitive impairment was defined.

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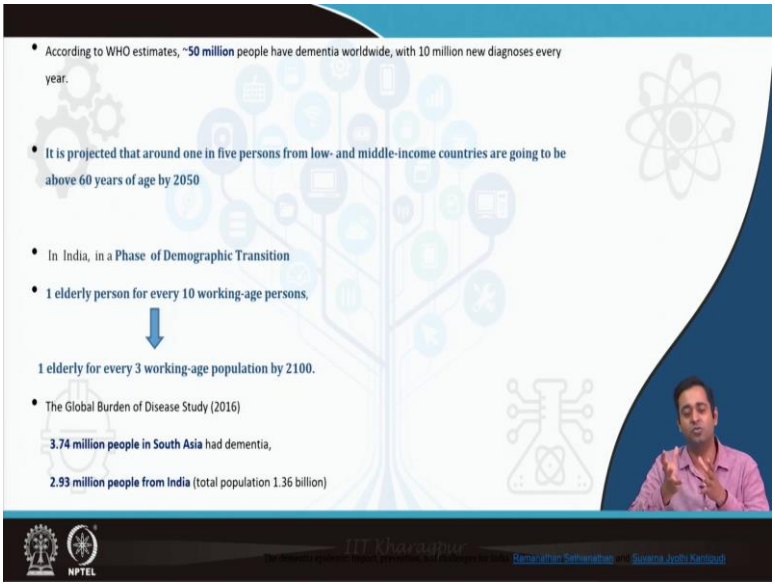

According to WHO the presently the scenario is that 50 million people across the globe they are suffering from dementia each and every year you have 10 million cases which are being diagnosed it is projected that in low middle income countries or (())(05:10) countries, this is going to increase further by 2050 and specifically talking about Asia and in India in particular, we in India are in a phase of demographic transition, it will be astonishing and surprising for you also because, yes, we are a youth population, the country actually belongs the primary population of our country's youth.

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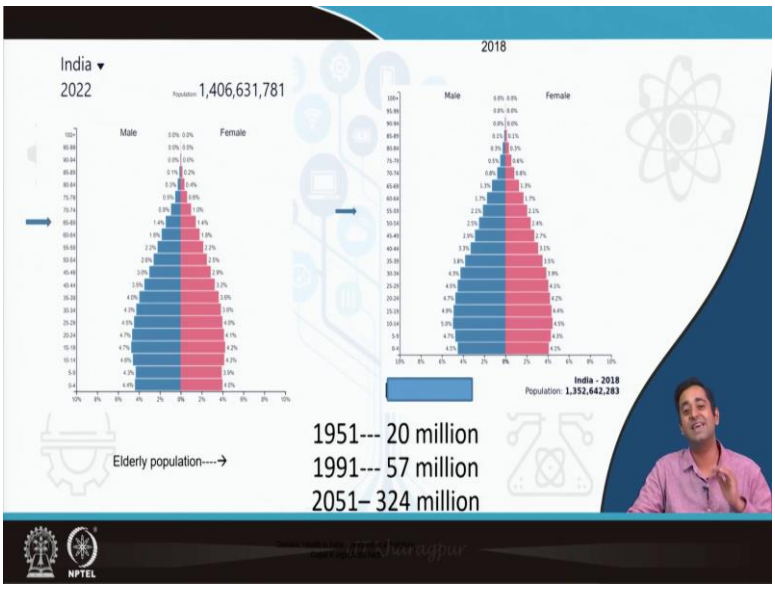

But if you see the figures from last four to five years, there has been an increasing trend of the old age population which is on the rise. So, from last four figures from last every 50 years

like five decades, in 50s, it was 20 million the elderly population which is on the rise which is increasing sequentially 20 million in 1951, 1991 it began with 57 million and it is expected to rise 324 million by 2051. So, that is how we should be aware of this fact.

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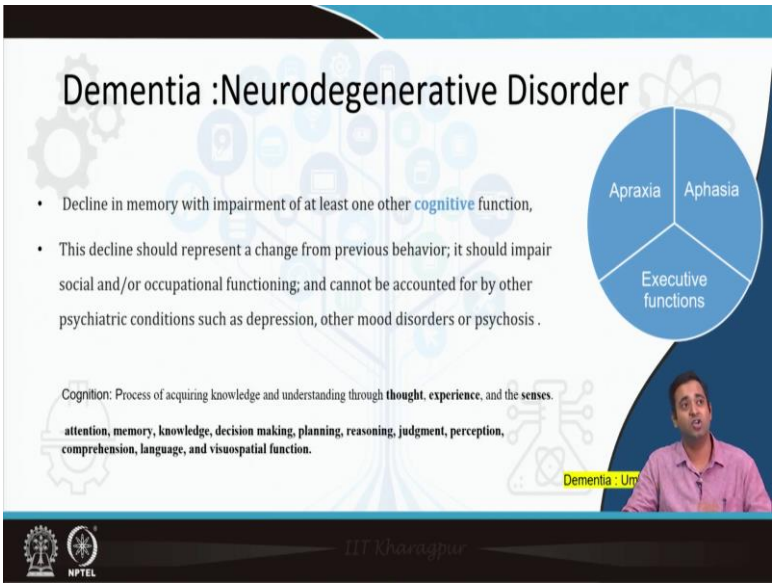

Now, what is dementia? Dementia is a neurodegenerative disorder which basically affects three main domains you have apraxia agnosia and executive functions are impaired. Now, what is an apraxia, agnosia? Apraxia is when your voluntary functions of skilled movements are not being performed, even though you have a normal motor and sensitive function of your body or normal it is preserved. But even though you are not able to perform it.

Agnosia is likewise is where you are not having your sensory stimulations, you are not able to you are devoid of your senses even though the patient is not even though the patient is having desire or is or it is seen as faculties are absolutely normal. What is aphasia? It is an inability on the part of patient to have a speech output.

And the executive functions, executive function means you are walking you are running, you are moving your limbs, your calculations, your arithmetic problems, you are analyzing ability, your comprehension, all these issues, this is affected and there is decline in or this decline should represent a change from previous behavior, it should impair social and occupational functioning and cannot be accounted by other psychiatric conditions such as depression, or mood disorders or psychosis.

Now talking about cognition, your cognitive function, cognition is actually a process of acquiring knowledge, understanding through thought and experiences and the senses like with the help of senses, you are perceiving the environment.

So, it is it involves all those processes such as attention, comprehension, judgment and analytical skills, your problem-solving abilities, your reasoning judgment, all those things visual spatial ability, you are seeing, you are perceiving the surroundings, your two-dimensional ability of visual visualizing your three-dimensional ability of visualizing everything covered under the cognition.

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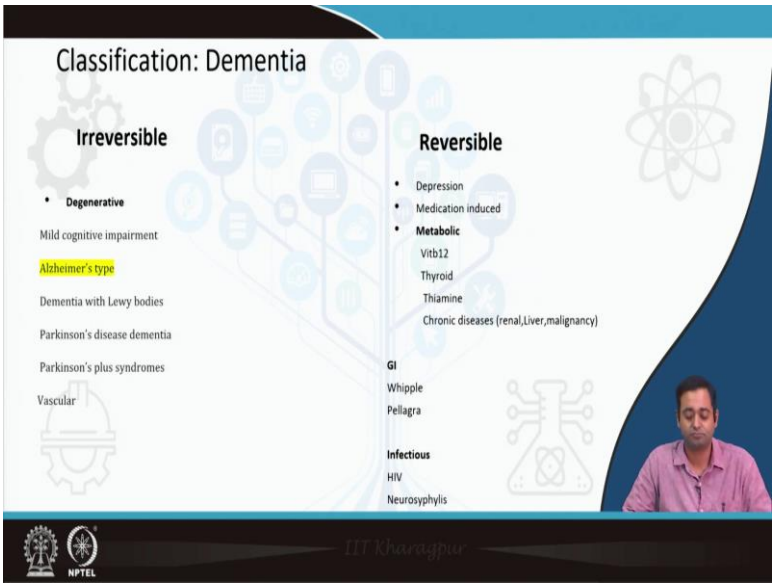

Let us talk about the classification of dementia. We have, the normally there are reversible and irreversible, dementia so irreversible dementia that those were the treatment is not possible. Only palliative treatment is given for reversible dementia. These they basically occur because of deficiency in some micronutrients present in your body. So, for most, this is treatable. So, most commonly is vitamin B12 deficiency dementias.

You have thiamine deficiency, thyroid deficiency, TSH levels, T3 and T4 levels are decreased or increased. It is also related with chronic diseases like liver, kidney. One most important entity which should be differentiated or delineated with dementia is depressive pseudo dementia, which is happening in geriatric age group, old age group, where the patient activation suffers from depression and the symptoms characteristic features they actually mimic those present in the dementia.

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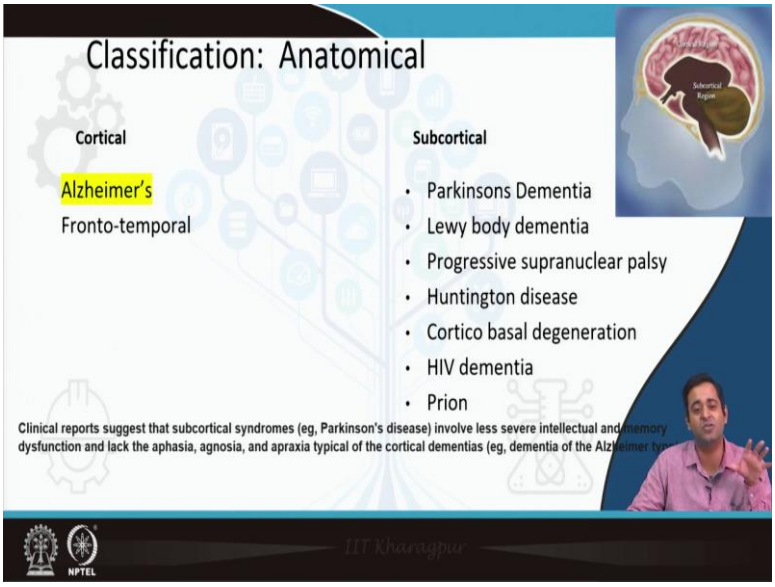

So, let us look at the anatomical classification of dementia where you have a cortical group of dementia then you have a cortical subcortical group of dementia, cortical is where it basically involves the cortical lobes that parietal temporal, occipital frontal lobes and the subcortical areas like basal ganglia, all those areas.

Parkinson's disease, dementia is the prototype of subcortical dementias. And in subcortical dementia, the severity the affected feature is less the patient is having less affected in impairment of those apraxia, agnosia, aphasia whereas in cortical dementias like fronto-temporal, temporal parietal, all those kinds of dementia, Alzheimer's fronto-temporal there is more the severity is more where apraxia aphasia agnosia's are more commonly involved.

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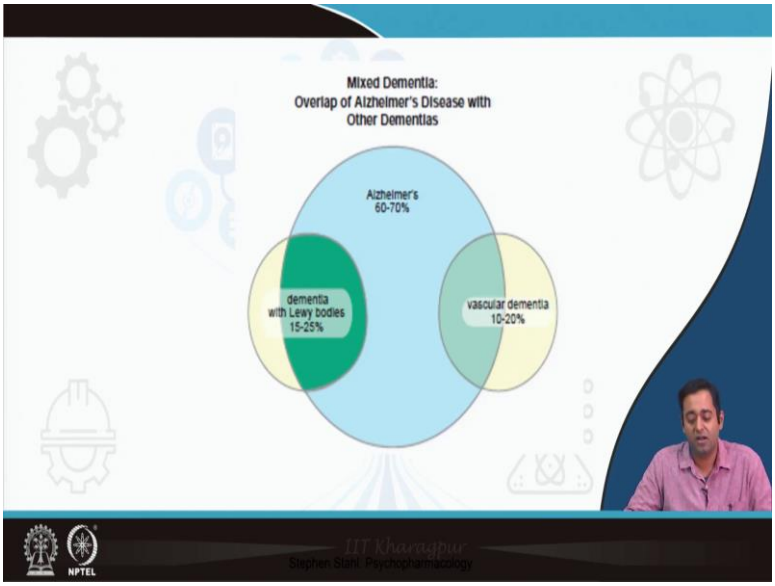

Alzheimer's involves a chunk of dementia group, second is your lewy dementia and the last is vascular dementia.

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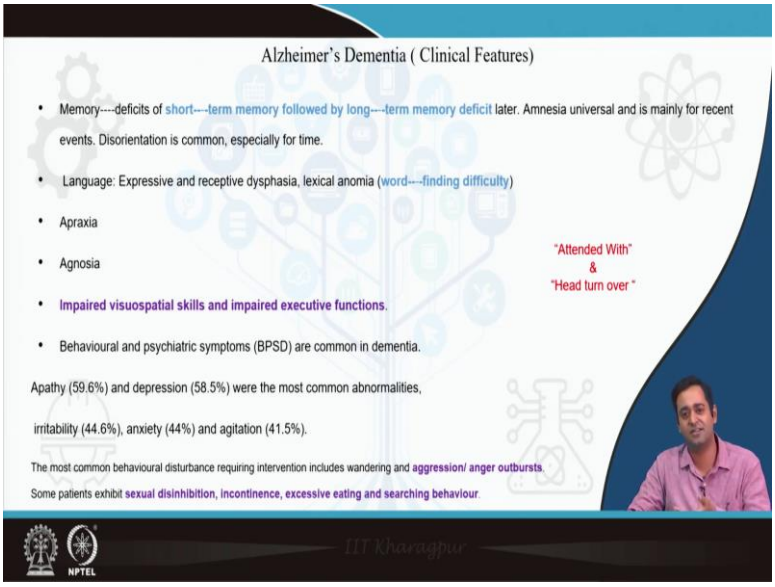

Let us look at the features of Alzheimer's dementia. Now initially, there is a short-term memory deficit which in later years, it progresses and involves your long-term memory, short term memory means patient is not able to remember what he or she has eaten last night, who she or he has met within last six hours or last night or the previous day. So, he might have like the person who might be suffering from dementia at home or at wherever you are seeing those old age problems.

Like the patient might be telling that I have not been given my meals even though the caregiver who is taking responsibility of the patient has given the meal just few minutes or some few hours back, he the patient, sometimes tell I have not taken tea please give me tea. But the fact of the matter is that the caregiver tells that I have already given tea some few minutes before some few hours before. So, there is recent memory deficits present in the patient, which is more obvious and manifested more clearly.

Among time, place and person the disorientation is more specially for the time the patient becomes disoriented with respect to time that is he does not know he or she does not knows what time of the day is it is it morning is it evening is it afternoon. So, there is disorientation there is expressive as well as receptive dysphasia patient is not able to express as well as comprehend, so receptive as less expressive problems are present on the part of patient.

And there is word finding difficulties for many of us, who of us have experienced this one or either of our family members have like experience have suffered from these problems or are still undergoing these problems, like in our sentence, or if they are narrating a story, they tend to forget the names of a shop, they tend to forget the names of the person of the family itself, they tend to forget the names of your important accounts, bank accounts, their telephone numbers, it is very commonly seen.

So, there is word finding difficulties leading to lexical anomia, apraxia, agnosia. As, we all know, it is like not able to perform skill movements, even though your voluntary functions are spared, and agnosia, you are not able to have those sensations, even though your mental faculties and all those things are normal, the desire is there, but you are not able to do that. There is impaired visual spatial skills and impaired executive functions, like I told you the arithmetic ability, the judgment, the analytical skills, the reasoning power, all those things are affected grossly.

Then there are most common abnormalities associated with the dementic people these are apathy, depression, agitation, anxiety and irritability. Now, why is this apathy? Apathy is there because the patient is not able to express his problems because he is not able to remember all those like normal names word finding difficulty, he is not able to remember his address of the house where he or she is living, he is not able to remember the name of his family member.

Now, the insight is there, the patient realizes that why suddenly or why in due course of time in few years or in few months, this has suddenly happened, why he has become incapacitated. So, that is why there is this depression, this irritability, this apathy, which develops on the part of patient.

The most common behavioral symptoms is disinhibited behaviors, now when the patient is having dementia, this particular behavior is actually very annoying for family members or it creates a sense of shame, embarrassment, the person actually opens his clothes in front of other family members or who are strangers, he does not realize this or there is the loss of rationality of the situations where you have this notion that, I have to behave in a certain way in front of others.

So, this thought process is actually distorted your cortical lobes the innovation, which the prefrontal cortex we are actually having previously over the subcortical areas is disinhibited.

So, that is why this occurs. There is anger, aggression, out anger, outbursts. Now some patients have incontinence of emotion that is sudden laughter pathological laughter.

Now, what is this pathological laughter? Pathological laughter occurs wherever there is a conversation going on with a dementia with the person suffering from dementia with a normal person. If a question is asked to a demented people, he would not be able to give specific answers to that and suddenly, he realizes that I am not able to remember which is being asked for so, therefore, he gives us hidden laughter that is called a pathological laughter that is in a so high patient intensity that the person who is staying around or who is staying with the person feels embarrassed or sometimes annoyed also.

There is searching behavior, because there is never a deficit he does not remember he goes on and searches the entire house for the possessions of his or her that somebody has kept it somewhere else and please give me, I am unable to find it. He actually gives, he actually complains that this particular possession of mine, my mobile phone, my purse, might somebody has taken it, you have taken it some my family members, my son has taken my grandson has taken it. So, there is a searching behavior.

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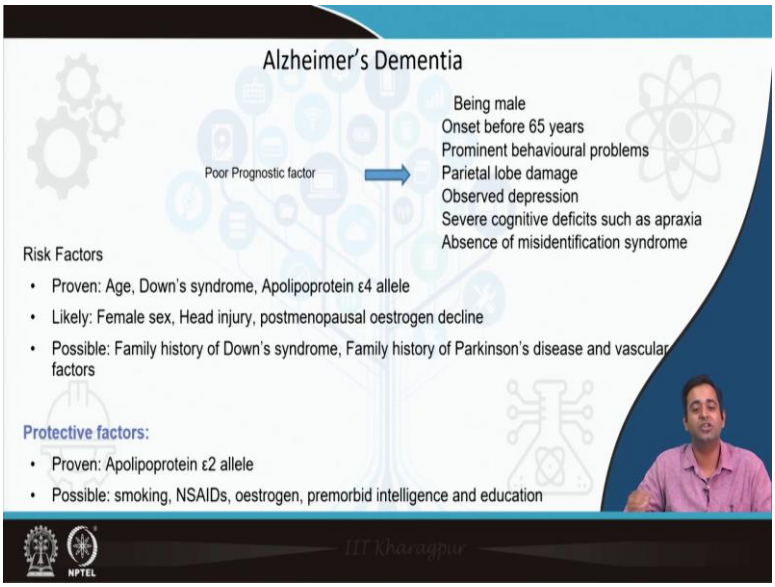

What are the poor prognostic factors? Male onset before 65 years prominent behavioral problems, parietal lobe damage, observed depression and severe cognitive deficits. What are the risk factors? There are basically proven likely and possible risk factors, possible is the family history of down syndrome and families of Parkinson disease with vascular factors that

is stroke hemorrhage in the past. Likely factors are female sex, head injured or postmenopausal oestrogen decline.

And proven factors are Apolipoprotein e2 allele with more than 55 years of age and down syndrome. What are the protective factors? These are Apolipoprotein e2 allele and possible factors are NSAIDs, premorbid intelligence and education the level of education attainment.

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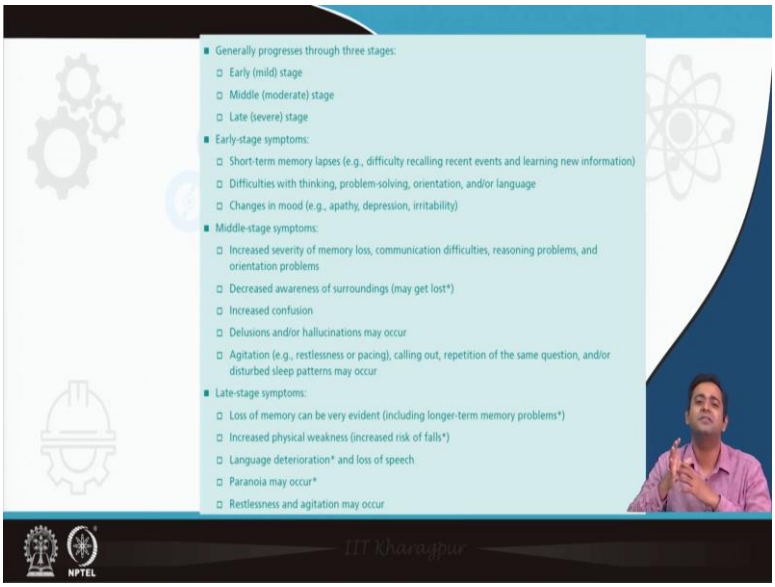

Now, this dementia, Alzheimer's dementia progresses through three stages mild, moderate, and severe. In mild stages, your short-term memory lapses are very of a very mild nature. So, the problems of day to day life is very meager it is the patient actually carries his normal day to life activities without any difficulty. What happens in middle stages? It went on and progresses to a severity, the intensity of the problem increases in the middle stages. There, he has lots of confusion, decreased awareness of the surroundings, he altogether forgets his address of the house, there is severe memory loss.

So, initially, where there was recent memory deficits now, it probably should progress to develop a remote memory problems also, where he has like some 10-20 years back or whatever places he had been, what kind of work he used to do when he was when he got married. When was the first child he got, who is like, 10 or 20 years back, where was he living. Those memories start to get affected in middle stages and in severe stage, the patient actually becomes bedridden. There is hallucinate experiences patient can have delusions as well, there is a restlessness and severe paranoia.

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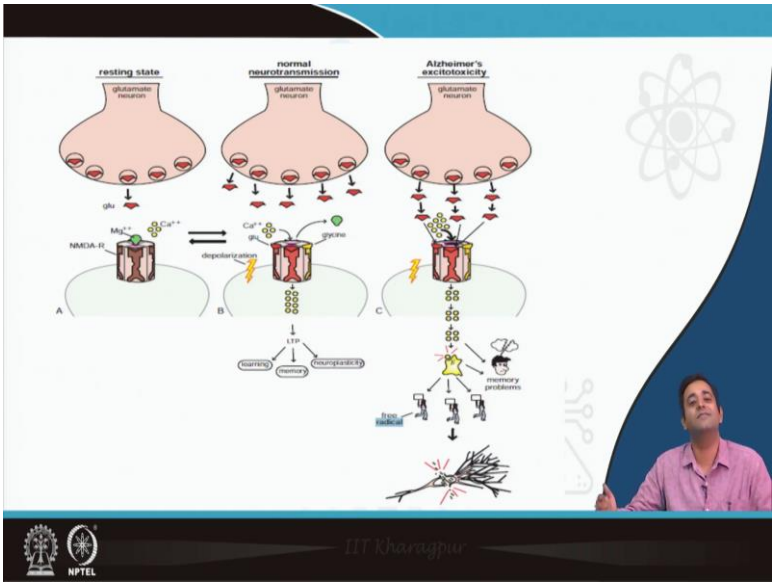

Let us look at the process, the mechanism of Alzheimer's toxicity. Why it is happening? How does the glutamate levels it expands and lurching your results into free radical accumulation, which further progresses and damages the long term potentiation and divert vertical responses, which creates problems of memory and all those things.

So, in resting state, normally, the glutamate neuron has NMDA receptors, there are basically three kinds of receptors for glutamate. You have NMDA, AMPA and Kainate. But, this glutamate neurons. This Alzheimer's toxicity specifically they occur in the NMDA receptors.

So, in NMDA receptors for a normal propagator impulses in a normal neuronal transmission, for impulse to be propagated, the glycine and glutamate has to join simultaneously in the NMDA receptors, following which the calcium channel plugs it opens and the calcium channels are there is invert progression of calcium ions, which leads to propagation of the nerve impulses.

Now what happens in this Alzheimer's toxicity? The impulses which is present in the Alzheimer's dementia, where the NMDA receptors are actually over functioning where the turnover of the glutamate is affected, the transporters, the glutamate transporters, they are not allowed to reuptake the glutamate from this articulate, which results in increased accumulation of glutamate which results in toxicity. So, that can lead to memory problems, and neuroplasticity does not occur which leads to diverse biological responses.

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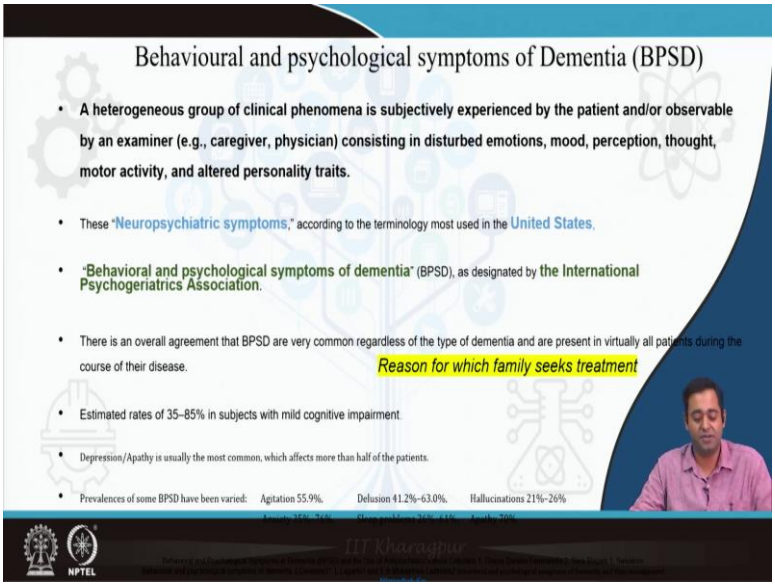

Now, what is this BPSD, behavioral and psychological symptoms of dementia. BPSD is the primary reason for which the patient's caregiver seeks treatment. It is a heterogeneous group of clinical phenomena subjectively experienced by the patient and the clinician who is treating consisting in disturbed emotions, mood, perception, thought, motor activity and altered personality traits.

These neuropsychiatric symptoms according to terminology is being used most commonly used in US. So, neuropsychiatric word is used in US and behavioral and psychological symptoms of dementia is commonly designated by the International psychogeriatric Association.

Now there is an overall agreement that it is very common regardless of the type of dementia this BPSD. And, it is estimated to be somewhere around 35 to 85 percent of subjects with MCI. So, we have developed this notion that MCI people cannot have BPSD, no MCI people can also have BPSD. Depression and apathy is the most common, which affects more than half of the patients who have dementia.

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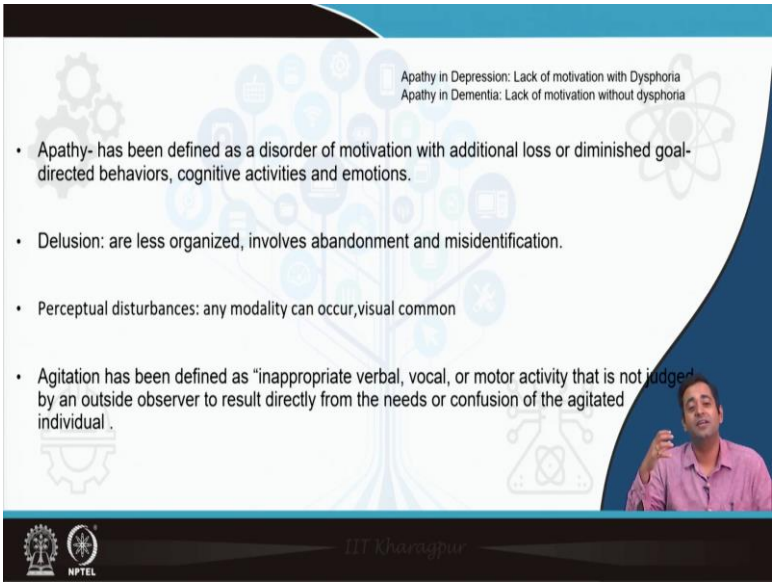

Now, this apathy is also seen in depression and apathy is also seen in dementia. But what is the differentiation there is a lack of motivation with dysphoria and depression and there is lack of motivation without dysphoria and dementia. What is apathy? Apathy is a disorder of motivation with additional loss or diminished goal directed behavior. Cognitive activities and emotions and delusions also occur in dementia, but here the organization of the delusion is not that severe. Whereas in schizophrenia, the delusions are very much systematized organized, crystallized.

Perceptual disturbances can also occur, mostly visual hallucinations are seeing an agitation on the part of patient which is seen in Alzheimer's dementia is basically because patient is not able to express his problems that now he is not able to remember the names, word finding difficulties, he is not able to tell exact words, he is not able to tell there is expressive problems of speech. So, that leads to agitation, irritability, and that is manifested very commonly.

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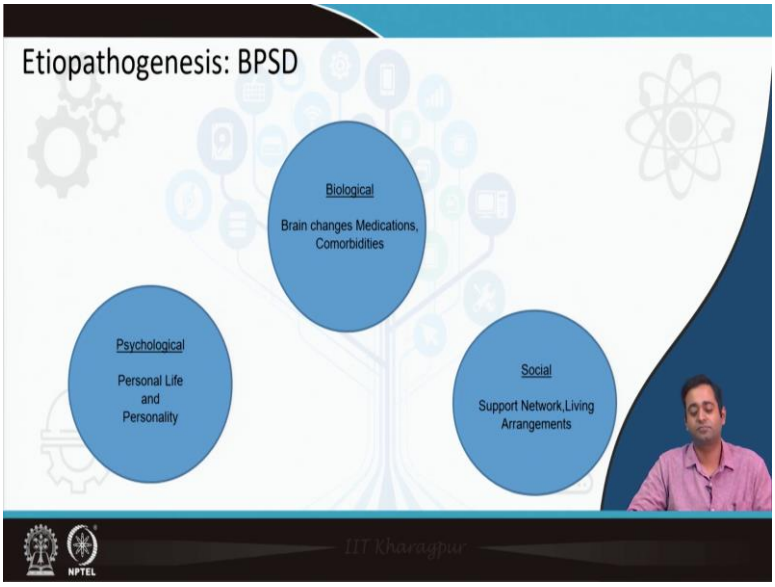

So, what is the pathogenesis of BPSD behavioral and psychological symptoms, basically three domains, psychological, biological, and social. Social is when you have poor support systems, you do not have enough, you do not have a good caregiver looking after the patient, the living arrangements at home where it is most comfortable for the patient to have his own belongings nearby, his own family members who can have emotional warmth, the feeling of cohesive cohesiveness in the family.

Biological is you have predisposed the genes which are there which makes you more susceptible to when in the later ages went where the patient went on and develops dementia. And sometimes it is the anticholinergic medication also, that can give rise to it with some comorbidities of physical like hypertension, diabetes, all those things. And psychological problems of personal life and personality. There are some issues related to psychological life which also adds to the problem of dementia.

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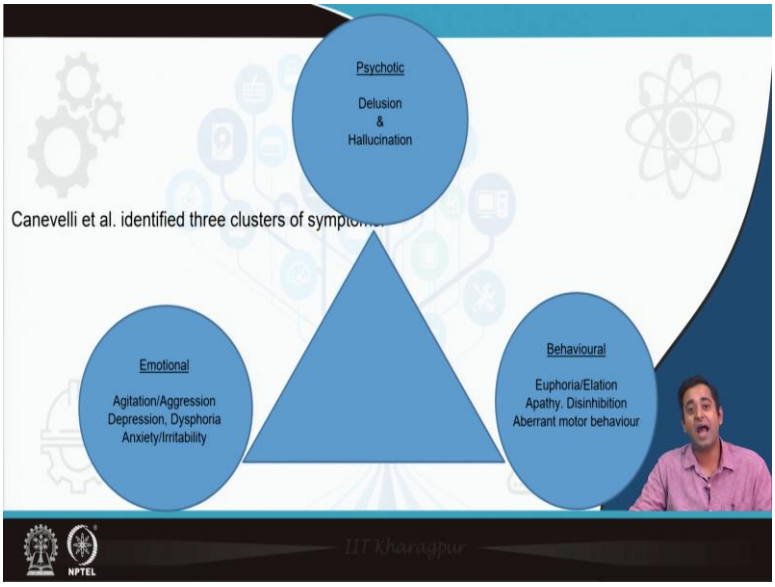

Canevelli identify three clusters of symptoms. These are basically psychotic, emotional and behavioral. Psychotic, very well, delusions and hallucinations are seen. In emotional problems there can be agitation, irritability, dysphoria, anxiety, and in case of behavioral issues, you have disinhibited behavior, apathy, and abnormal motor behavior is seen.

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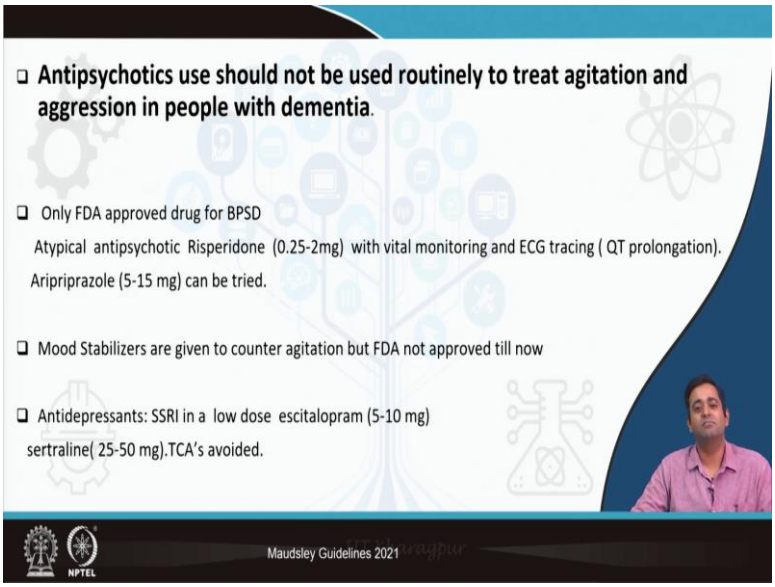

In order to treat this condition, anti-psychotics can be used but it is not used routinely to treat agitation. Only FDA approved for BPSD is risperidone and aripiprazole. Risperidone is used with ECG tracing because there is they are notorious to cause QT prolongation leading to cardiac arrhythmias.

Mood stabilizer given to control agitation but they are not FDA approved till now. Evidences are there that they give improvement and relief of symptoms to the patient. Antidepressant SSRI in a low dose and TCA's are mostly avoided due to cardiac related issues.

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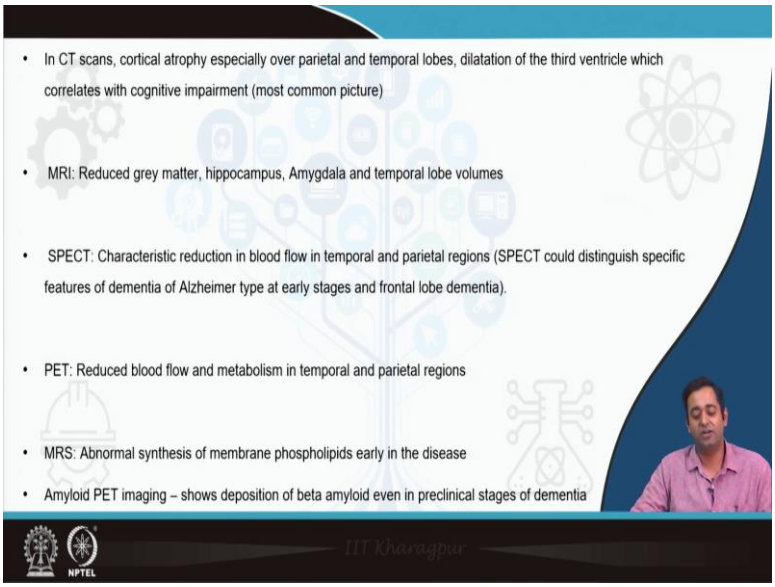

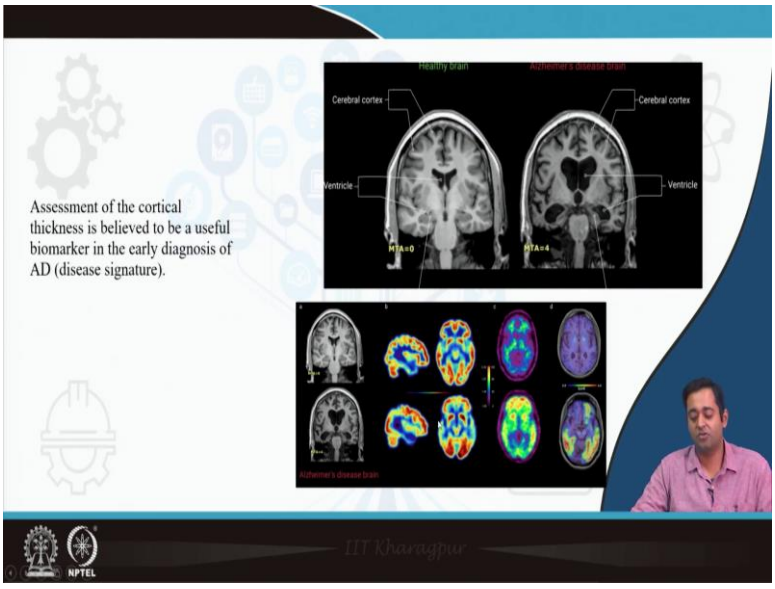

Let us look at the radio imaging. The findings where the patient can manifest with there is cortical atrophy especially over parietal temporal areas and dilatation of third ventricle which correlates with cognitive impairment. So, you see, there is this healthy brain and this is dementic brain. There is ventricular dilatation of the patient, thinness of the cortical areas, thinness and there is deepening and deepening of this (())(26:01). So, there is cortical atrophy dilatation of the cerebral ventricles and thinness of the cortical areas.

The single photon computerized tomography, if characteristic, there is characteristic of reduction in blood flow in temporal parietal regions. Now, this is actually helps in delineating Alzheimer's type and frontal lobe dementia's in PET scans. There is reduced blood flow metabolism in temporal and parietal regions. And, amyloid PET it shows deposition of beta amyloid even in preclinical stages of dementia. As you can see, accumulation of amyloid in PET scans.

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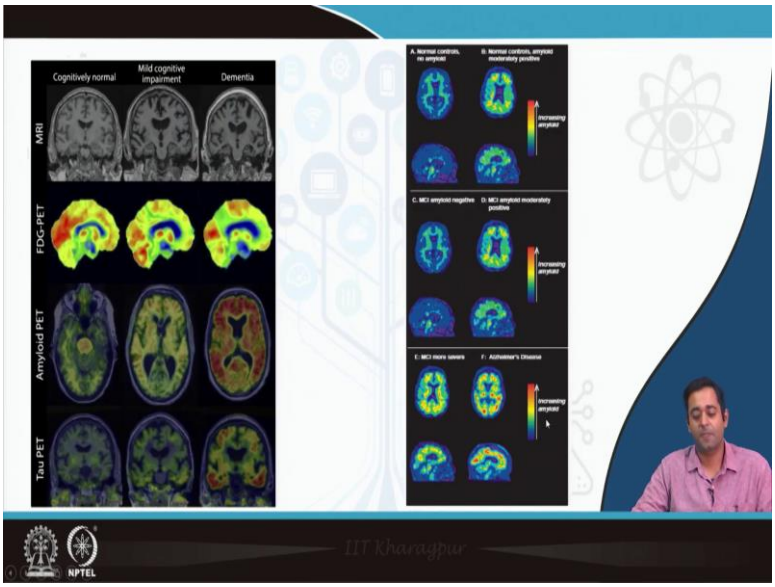

Here, you have sequential involvement normal brain MCI and dementia there is sequential degradation, you can see there is sequential dilatation of the cerebral ventricles and there is sequential involvement of the cortical atrophy is deteriorating sequentially.

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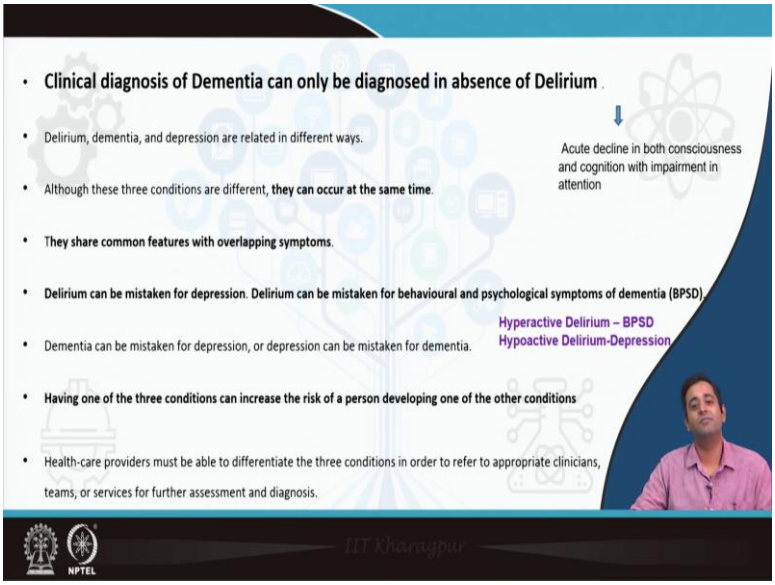

So, what are the differential diagnosis that the patient can have rendered while you are dealing a case of dementia, delirium and geriatric depression? So, these three features actually they overlap. So, one must be careful when we are dealing the patient with dementia patients can have symptoms of delirium, and can be suffering from depression also.

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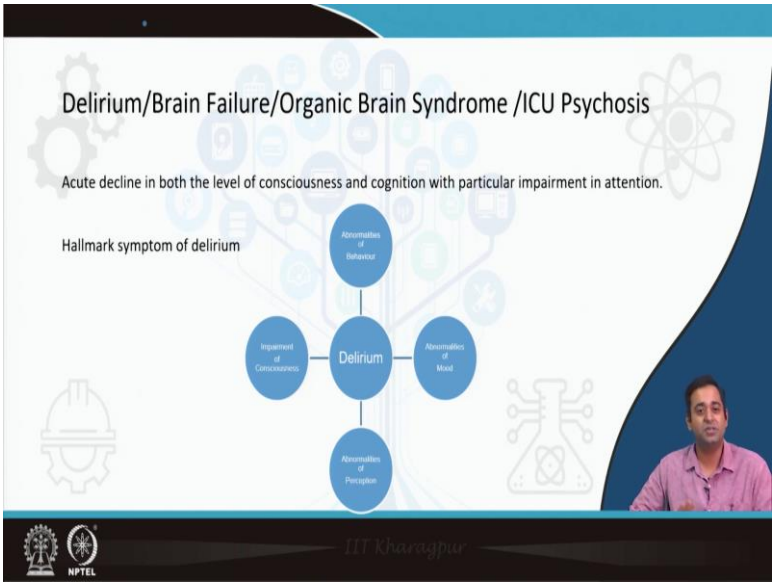

So, what is the delirium? Delirium is actually a decline in both consciousness and cognition with particular impairment in attention. What is the hallmark? Four hallmark symptoms, there is impairment in the mood; perception, sleep, behavior and consciousnesses.

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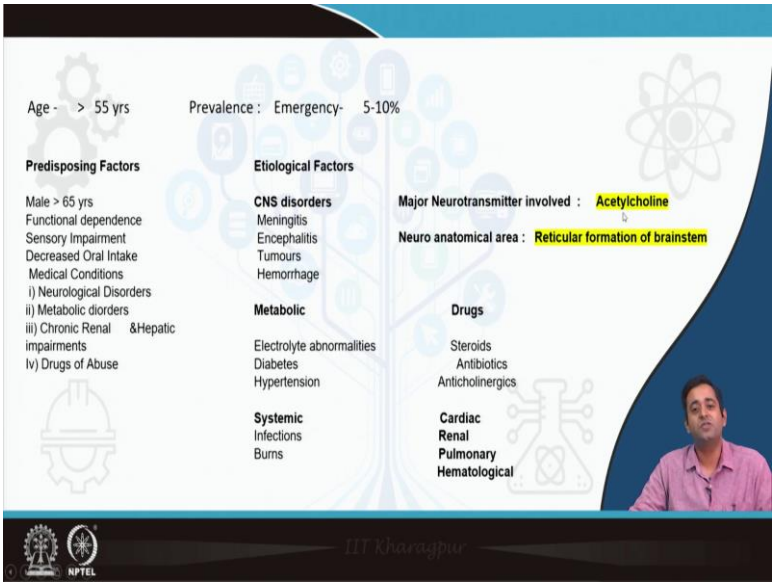

The predisposing factors being male more than 65 years, they are sensory, if there is sensory impairment, visuals, taste, gustatory all those things. Medical conditions like neurological disorders, metabolic disorders. Renal conditions like kidney conditions, liver conditions, can also give rise to delirium and drugs of abuse, especially the anticholinergic class of medications. The major neurotransmitter involved in delirium is acetylcholine and the structure is reticular formation.

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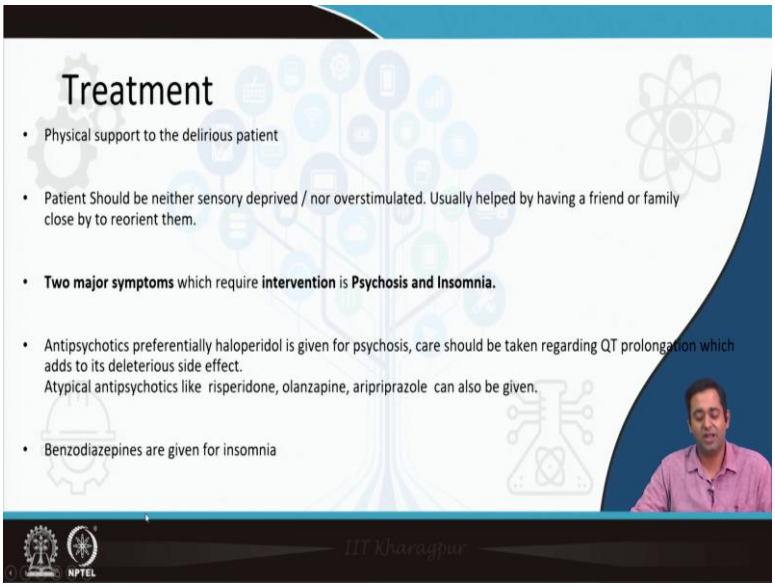

How to treat delirium? Basically, two things has to be intervene. One is the psychotic phenomena and other is the insomnia. So, psychosis is basically intervened by antipsychotics, specifically atypical antipsychotic because a psychotic are associated with antipsychotics

symptoms. So, that is why they are avoided. But, risperidone and this olanzapine can be given for the patient for delirium, and for insomnia (())(28:51) benzodiazepines are given.

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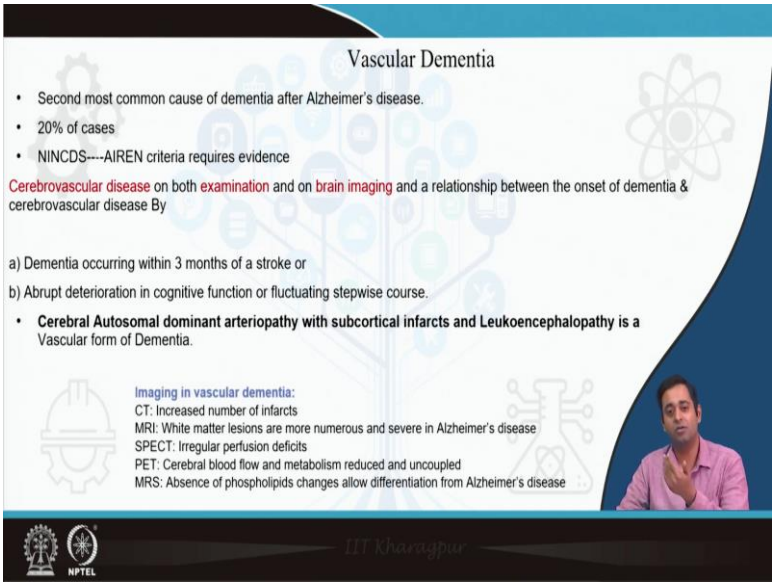

As see the other types of dementias vascular dementia, it is the second most common type 20 percent of the cases. So, the cerebral vascular disease on both examinations and brain imaging, they should be having one set within three months of the CVD. So, dementia occurring within three months of the stroke and there should be abrupt deterioration in the cognitive functioning or fluctuation in a stepwise manner. There is one entity called CADASIL that is cerebral autosomal dominant arteriopathy with subcortical leukoencephalopathy it is a vascular form of dementia.

Now in terms of a new imaging, you have increased number of infarcts there is white matter lesions which is commonly seen and that differentiates the Alzheimer's type. In terms of PET scans, cerebral blood flow and metabolism is reduced. And, in magnetic resonance spectroscopy, there is absence of phospholipid changes, whereas in Alzheimer's there are more phospholipid changes seen.

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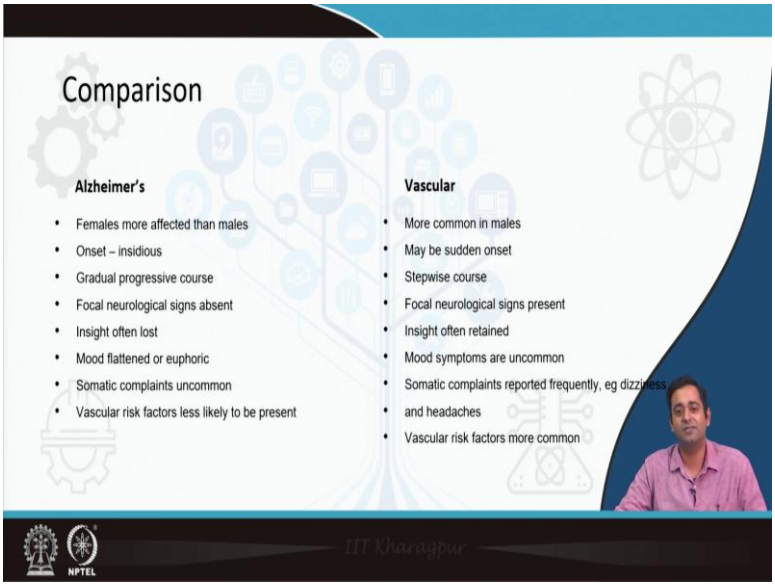

So, if you compare Alzheimer's and vascular dementia. Vascular is more sudden onset, Alzheimer's has a chronic onset gradual onset. Females are commonly affected in Alzheimer's. Vascular, it is more in male. Focal neurological symptoms are commonly seen in vascular dementia whereas it is absent in Alzheimer's dementia. Your mood symptoms are more in Alzheimer's, whereas it is less than vascular. And somatic complaints are uncommon in Alzheimer's or is more in the that is headache and all it is more present in vascular type of dementia.

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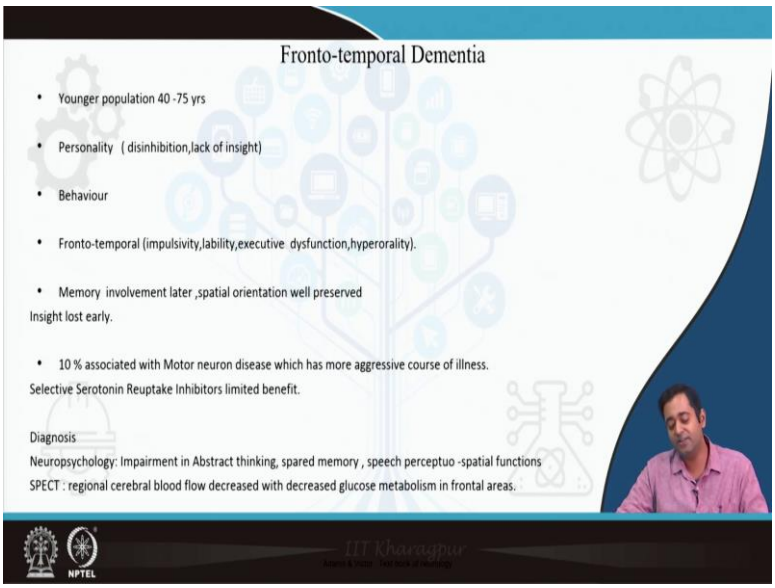

What is fronto-temporal dementia? Fronto-temporal dementia basically incorporates personality changes, behavior changes disinhibited behavior, impulsivity, memory involvement is later spatial orientation well preserved and insight is lost early.

So, if you compare with Alzheimer's dementia, the memory involvement is early whereas in fronto-temporal dementia, their memory involvement is later with sparing of the orientation there you have a disorder of the time which is most commonly involved. So, 10 percent of this FTD's they go on to develop motor neuron disease, which occurs during the aggressive course of the illness.

How it is diagnosed? It is with the neuropsychological tests there is impairment in abstract thinking, but there is impairment of the memory which occurs in later part of the disease. And in SPECT, that is Single Photon Emission Computerized Tomography. There is a regional cerebral blood flow decreased with decreased glucose metabolism in the frontal areas.

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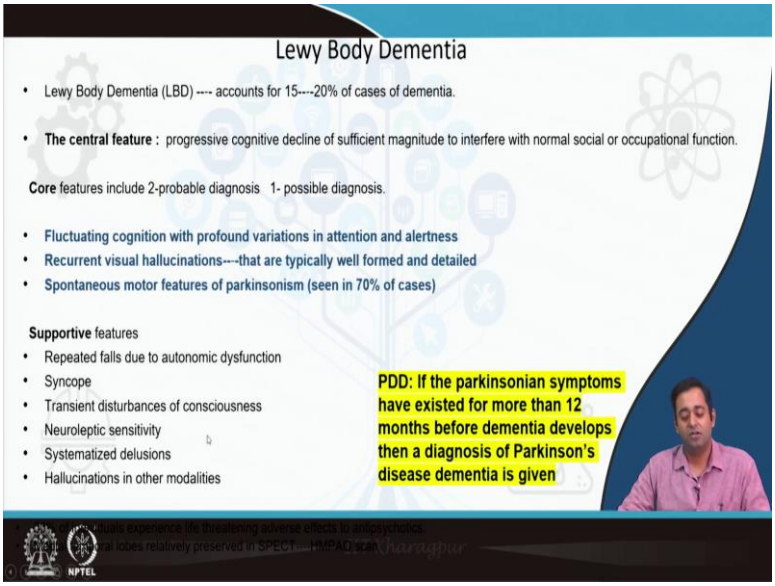

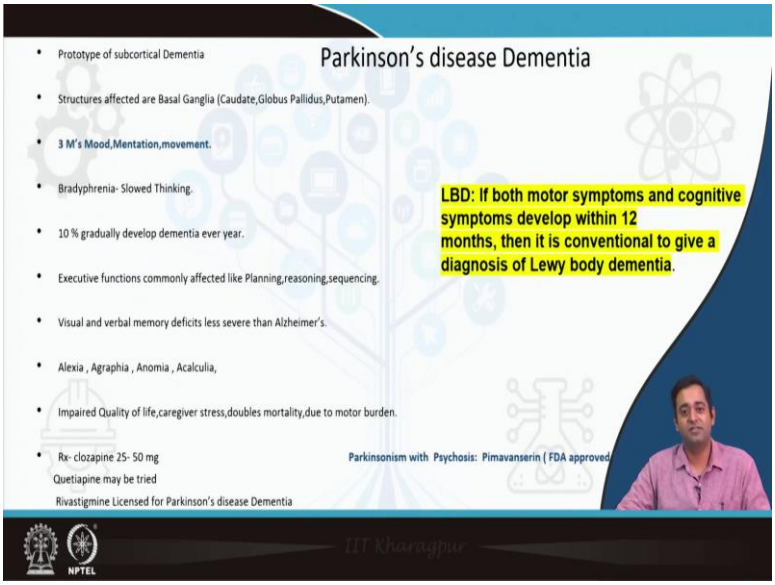

Now, two more entities that is Lewy body dementia and Parkinson's disease dementia that has to be differentiated. Lewy body dementia you have tried mood mentation, Parkinson disease dementia you have mood mentation and movement. Here in the Lewy body dementia you have fluctuation in cognition recurrent, visual hallucinations and Parkinson disease . So, these three features has to be looked out for.

Associated with sensitivity neuroleptics, the anti-psychotics they are more prone for extrapyramidal symptoms. They can have syncope, transient disturbances of consciousness, neuroleptic sensitivity as I told you, and there can be hallucinations of other modality.

So, how do you differentiate Parkinson disease dementia and Lewy body dementia? Parkinson's disease dementia is when you have Parkinson's symptoms before 12 months following onset of dementia, so that is it is Parkinson's disease dementia likewise, for Lewy body dementia, if both motor symptoms and cognitive symptoms they develop within 12 months, then it is convention to give a diagnosis of Lewy body dementia.

So, for Parkinson's disease dementia, executive functions are commonly affected like planning, programming, reasoning and sequencing, visual verbal memory deficits less severe than Alzheimer's and that is impaired quality of life because of the movement and as well as dementia both things are affected, which is making life more miserable.

Now, since there are movement disorders which is affected with the extrapyramidal symptoms, it is affected and is the antipsychotics which blocks dopamine receptors due to receptors are not commonly implicated. So, we have a drug which is FDA approved very

recently that is called Pimavanserin, which is a 5-HT2C inverse agonist. So, it has a different mechanism of action as other atypical antipsychotics has.

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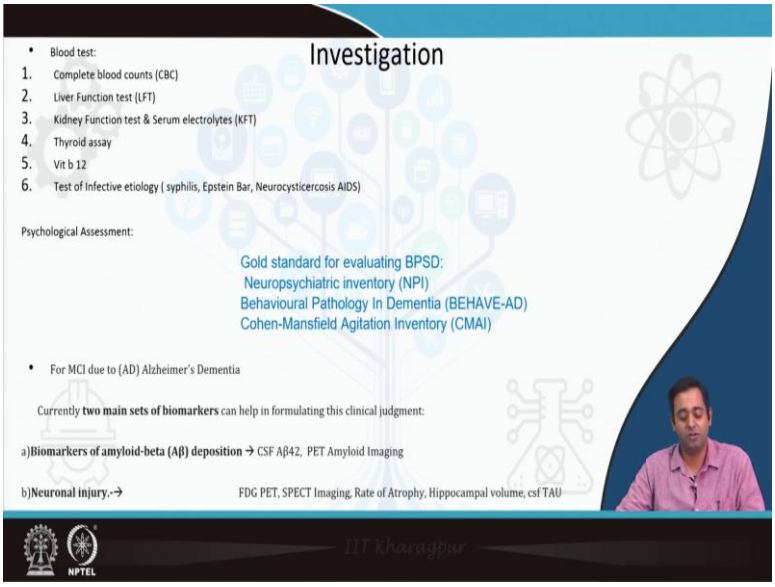

What are the investigations? The normal relevant blood investigations at complete blood counts, kidney function tests, liver function tests, thyroid assays and all psychological assessment. Gold standard for evaluating BPSD is new psychiatric inventory. For mild cognitive impairment due to Alzheimer's dementia, we have a specific test which tells that these patients have MCI they can develop Alzheimer's dementia.

So, there are currently two sets of biomarkers. Biomarkers of amyloid beta deposition and neuronal injury for amyloid beta deposition. We have beta amyloid imaging and CSF A beta 42 for neural injury we have SPECT imaging rate of atrophy is actually looked for and hippocampal volume.

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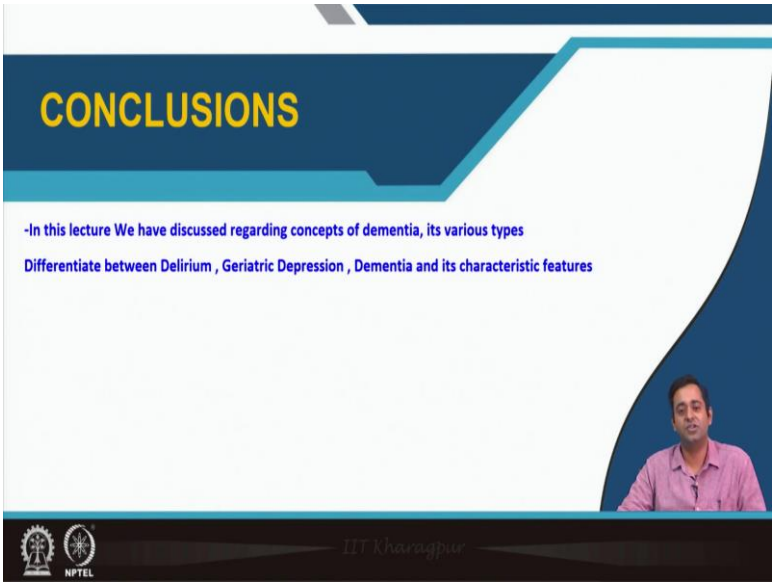

So, in this lecture, we have discussed regarding the concepts of dementia is various types differentiated with delirium, geriatric depression, dementia, and its characteristic features. Thank you.