[MUSIC PLAYING]

DANIEL VARON: I'm going to talk to you but neurocognitive disorders, and I'm going to tell you about how to approach patients that come in with cognitive dysfunction. So this is kind of an overview-- let me see if-- this is an overview of the talk. And what we'll cover is, initially, how to determine if the patient has cognitive decline versus just cognitive impairment, some of the diagnostic criteria that we would use, and then some of the ideologies of the neurocognitive disorders that we most commonly see.

So in normal aging, there'll be some kind of dysfunction over time. So when you get to 40, your cognitive abilities kind of peak. Then you stay there for a while. And then when you get to late 50s and early 60s, then there seems to be a slow decline that is very mild, but it's there. And it's primarily in areas of attention, presence, speed and working memory.

Now when you see patients in the clinic, they'll come in and say, I'm having some difficulties with memory or other cognitive functions. And you need to determine are they having some problems or not. So how do you approach that question? What do you ask them, and how do you figure out what's happening to them?

So, ideally, what you want to do is first figure out are they having cognitive impairment. So a lot of people will come into a primary care clinic and say, I'm having problems with my memory. But if you look at their background, they might have a chronic psychiatric illness. They might have a history of substance use. They might have a history of traumatic brain injury or they might have a history of mild intellectual disability. And on testing, they will not do that well.

But that doesn't mean they're declining over time. Like you see in the second graph, they're not going downhill over time, as that curve shows. So you need to determine if they're having cognitive decline, is the next thing you need to do. And, most importantly, you need to figure out do they have mild cognitive impairment or do they have a dementia or a major neurocognitive disorder. So what's that line? What divides people from the area that they have mild cognitive impairment from the people that have mild dementia? Well, it's their functionality.

So if you're having cognitive dysfunction in one or two areas and that is leading to you requiring help for activities of daily living, instrumental activities of daily living so you no longer can live independently-- those people have crossed that line because they're no longer independent. And they now have mild dementia. If that progresses, they'll develop eventually moderate or severe dementia. So that's important, trying to figure out if they're declining or not.

Now you have to keep in mind that some people will have a high cognitive reserve. So they might coming to the clinic and they say, I'm having memory problems. And you test them, and they don't seem to have problems objectively. Your MoCA is 30 out of 30. Those people might have a high cognitive reserve. And eventually, once they exhaust the reserve, they start to decline. And they actually might decline quicker that other people that have lower reserves.

So you see here, people that have a lower reserve, they kind of go downhill slowly. The people with high cognitive reserve might go down a little bit more quickly. At the end, both groups end up at the same point. Some families will tell you, you know, my dad just wrote a book not long ago he was doing so well, and now he's declining so quickly. Well, that person might have had a high cognitive reserve, and that's the reason you see that kind of steep decline. So keep that in mind because that can alter your perception in terms of how the person progresses.

Now, obviously, there are multiple causes for cognitive disorders. And so your task is trying to figure out-- once you figure out if they're declining, if they do have cognitive impairment, the question is what's the etiology of this condition. So you need to try to figure that out.

And then you also need to keep in mind, when you're evaluating a patient, where you're evaluating that patient. So if you're doing it in primary care, it turns out that a lot of the people that come to primary care with mild cognitive impairment don't have a neurocognitive disorder. They actually have other conditions that actually don't progress. They just stay there.

So this is a slide that Mary Ganguli provided for me. And she kind of suspected this all along. And, actually, this has been corroborated more recently in studies with newer pathological findings. And, basically, what you see is that if you see patients in an Alzheimer's disease research center, a lot of those patients with mild cognitive impairment do have Alzheimer's disease or some neurodegenerative disorder.

But if you see them in primary care, that population is a little different. You have some people that do have a neurodegenerative disorder. But a large portion of that population might also have some other condition that presents as mild cognitive impairment. But they might not progress over time. So you need to follow them over time to try to determine whether or not they're progressing. So that's important.

So how do you go about it? So you need to do pretty good evaluation initially. You need to ask the family and the patient, when did this start? What kinds of symptoms did you present with? Was it memory, behavior, language? And you really need to dig and probe the family. Because sometimes they will tell you, this started one, two years ago. And then you ask some more, and they said, yeah, he/she got lost five years ago. And so then you realize something else is going on. They've been compensating for a while.

And what kinds of symptoms were they having? And sometimes they miss things like behaviors or language or things like that. And then you realize that maybe that came first. And so you need to keep that in mind. In the medical history, obviously you want to find out have they had any trauma, have they had any history of stroke, obviously. Are they using substances or have they had a history of heavy alcohol use?

Also, if they're had a psychiatric history-- chronic psychiatric illness will come with cognitive dysfunction, that might be mild but is present. And, like I was saying before, it's kind of static in most patients. Then you do a physical examination, and you need to include a good neurological exam. And you need to evaluate to see if there's any subtle changes that would suggest previous strokes or vascular disease.

You want to look at their eye movement, make sure that you look at the vertical gaze, especially if they're falling because you're thinking of PSP. Or you want to look for Parkinsonisms. You want to check their tone, make sure that you know they're Bradykinetic or rigid, those kinds of things. And look at their gait, not only because of Parkinsonism, but also for things like to check for things like normal pressure hydrocephalus. All of those things can help you figure out what the patient has. So physical examination is really important. Make sure to include a good neurological exam.

I'm not going to talk about the labs because you guys know what to order. This is pretty clear, in general. It's not that complicated. But let's talk about cognitive testing and imaging, which are also important and often used in the evaluation of these patients.

So these are the cognitive areas that you want to kind of assess. And you do it in a different ways. Most people will use a MoCA or and EXIT or a SLUMS. The EXIT is something we use in our unit to evaluate more deeply into the executive function of the patients. Especially people with schizophrenia or other psychiatric conditions may have more executive dysfunction.

Language, memory, social cognition, things like that you want to explore a bit more. The MoCA is what we use most often in most clinics, but that's just a screening test, same with the SLUMS. You can do some assessments with the help of OT, for instance. You can ask them to obtain a KELS, so you can get a sense for how the patient is functioning, whether or not they're having difficulties with instrumental activities of daily living. And that can help you to determine have they crossed that threshold, are they now in the dementia range of the continuum.

You can also give people these questionnaires, like the FAQ or the PSMS, that are meant for the families to kind of rate how they're functioning. And you can use that to track people over time to see if they're declining. To the FAQ is for instrumental activities of daily living. PSMS is for basic activities of daily living. It's very simple, very quick. You can give it to the family, and you can keep track of how they're doing over time.

Memory centers will use the CDL, the clinical dementia rating scale, to determine the same thing, if people are declining or not, and see how they're doing over time. Some people might benefit from neuro-psych testing. And you don't send everyone to neuro-psych testing, but some of these patients could benefit from this, especially people that present with atypical symptoms.

So if you see a patient that don't quite fit the picture that you'd expect, then you think of neuro-psych testing. Also, if they present early or if they are progressing very quickly, think of neuro-psych testing. And people with a high cognitive reserve, because the things that you're going to do are not going to pick up on the deficits. So MoCA is going to be completely normal, but neuro-psych testing might show some of the deficits.

So in terms of imaging, that's the other thing that sometimes you see people will think about, and not necessarily order. So the American Academy of Neurology suggests that you should get some sort of imaging, structural imaging, so either a CT scan or an MRI of the brain in all patients that have neurocognitive disorders initially, when you first evaluated them. You can also use nuclear medicine to try to assess the patient and try to distinguish people that have atypical forms of AD from FTD.

And amyloid imaging and tile imaging are available, but those are not used clinically. Although amyloid imaging is approved for clinical use, it's not usually used for the evaluation of patients except in memory disorder centers. So let's talk about structural imaging for a second.

So if you do get a CT scan or MRI-- ideally, you would want to get an MRI. But let's say if you don't have the possibility of getting that. You just get a CT scan. But still, you would do the same thing for both. What do you look for?

It's important for you to look at the images because the radiological report is often very generic. It doesn't tell you that much. Unless you look at the images, you're not going to know exactly what's going on in the brain of the patient. You want to look at the general appearance of the brain. Look for atrophy. Is there generalized atrophy? Are the ventricles enlarged or not? Is there a lot of vascular disease? And are there specific patterns of atrophy?

And the more you look at the images, the more you realize that is actually a lot of information that you can gather from these tests. So I don't know if you can see that well, but these are two patients that I wanted to show you. On the left there's a patient who's 62, has some history of schizoaffective disorder, and some cognitive decline. On the right, there's a patient who's 70, has cognitive decline and late onset psychosis. And on the left as a CT scan, the right is an MRI. But you can compare them and see the differences.

And, basically, what you see is that the person on the left-- this is the medial temporal region. This area here, this is the temporal horn. And that is of normal size. When you look at it on the other side, you see that that's enlarged. So that reflects atrophy of the hippocampus in the medial temporal regions.

Same thing and the outer portion of the cortex, you see that the sulci are widened. And if you look at other sections, you see the same thing. You see the ventricles are enlarged. You see that there's widening of the sulci. And you don't see that on the other scan.

What does that tell you? That doesn't give you a diagnosis, but it just tells you that this patient on the left might be having these symptoms, cognitive symptoms, related to the chronic psychiatric illness rather than the condition is declining over time. The person on the right, on the other hand, might have something that is neurodegenerative. Again, this doesn't make the diagnosis. You have to put this in the context of the clinical picture. But it may help you figure out what's happening to the patient. So that's useful.

You also want to look at vascular disease. And you see here two examples of this. One with very mild vascular disease, perioventricular white matter disease, and the other one with more severe changes. You want to try to rate that. You want to say, is it minimal, mild, moderate or severe. And sometimes the radiologist will do that for you. But you want to kind of get into the habit of looking at it because then you can kind of make up your own mind about how much do you have there.

If you're going to diagnose someone with vascular disease, you need to look at the MRI or the CT scan. Because you need to have changes there. If they don't have any changes, they don't have vascular disease. That's picked up on the MRI or the CT scan. Otherwise, you cannot make that diagnosis.

You can also look for patterns of atrophy. And another reason resource centers people use this scale is to look at the hippocampus. But you can do it if you order the right sequence. And so, for instance, you can look at the size of the hippocampus in the cranial sections. And this is a scale that we often use in the ADOC in Miami, where you rate the size of the hippocampus. Here is no atrophy, and here severe atrophy.

And basically what this helps you with is to determine whether or not the changes in the MRI are suggestive of something that is degenerating the medial temporal region. The most common cause of that would be Alzheimer's disease. So if you have a patient that has a picture or a clinical presentation that suggests Alzheimer's disease, but has this on the MRI-- no atrophy whatsoever in the hippocampal region-- then you need to question the diagnosis.

You need to figure out is there something else that could be causing this. Could this be a different kind of dementia? Could there be other factors that are causing the cognitive decline? On the other hand, if you see moderate or severe atrophy, then that could support your diagnosis and might kind of help you figure out what are the next steps.

You need to be careful with the hippocampal atrophy in people that are older. Because as you age, you will have atrophy of the hippocampus. So people over 80 or 85 may have some atrophy, and that doesn't necessarily mean that they have Alzheimer's disease. So the younger the patient, the more significant when you find this kind of atrophy.

You can also look for atrophy more posterior regions, like the medial portions of the parietal lobes. This is called the precuneus, which is affected by Alzheimer's disease very early on, the posterior cingulate, and the lateral portions of the parietal regions. So those areas can be affected in patients that are younger that present with atypical forms of AD. Something called Posterior Cortical Atrophy or PCA can present like that. And they might not have any atrophy in the hippocampus, but they do have atrophy in those areas.

The radiologist is not going to call that. Unless you look at the images, you're not going to pick it up. And so if you see someone with this amount of atrophy-- and you see here this is the precuneus, and you can see the widening of that area. You see the atrophy and the widening of the sulci on the lateral portions of that. Then, that can help you kind of figure out the diagnosis.

Now other conditions can present with specific patterns of atrophy. So FTD sometimes finds atrophy of the Insula region. You see the symmetry here, so this is a person with non-fluent/agrammatical front temporal dementia. You see the asymmetry on one side. The left side is-- this space is opening up. You can also see atrophy in the anterior portion of the temporal lobe in semantic dementias.

And then, in FTD behavioral variant, you can see atrophy of the frontal lobes or more pronounced atrophy of the anterior pull of the temporal lobe on the right side. So if you see these changes, then you should suspect is this FTD. And what you do is you can get a PET scan to confirm or a SPECT scan to confirm your suspicion.

So if you want to get coronal sections and try to look at these things and get a better sense for whether or not there's specific patterns of atrophy, what you should get is an MRI without contrast, and you should-- the indication usually that we give the radiologist is cognitive decline. And we say we we want thin coronal slices with this specific sequence. And that's SPGR or similar sequence.

And you want to say I want to evaluate for patterns of atrophy. And, actually, you can ask them-- if they have software to do volumetrics, they'll do it for you. Actually, at Presby they'll do it for you. And this is what they'll send you. They'll send you a reading of what your patient looks like compared to the general population. And so they'll give you an idea about where your patient falls, and whether or not they have enlarged ventricles or the hippocampus or the frontal lobe or the temporal lobe is too small or it falls within the normal range.

And that can help you figure out they have a specific pattern that would suggest a specific condition. And they actually will send you a written report on that. So you can just get that type of MRI, and they will send you. So you don't have to be an expert at looking at images. You actually can get this kind of report, and that can give you an idea about what might be happening with the patient.

PET scans or SPECT scans can be very helpful, especially in those patients that I was telling you before, who present with a typical forms of AD or people that presents with FTD and you're trying to figure out what condition they have. So you see here, people with Alzheimer's disease will have a very specific pattern with parietal temporal deficits, while people front temporal dementia will have more anterior deficits with temporal and frontal hypo-activity. So that could be quite helpful.

This amyloid imaging, like I was telling you before, it's available clinically. Is quite expensive. Insurance companies don't pay for it, but it's used frequently in memory disorder centers to evaluate patients that are complicated, that don't have typical pictures. And those people can sometimes have-- young patients can have this to try to determine whether or not they have AD.

Once treatments for Alzheimer's disease become available, especially if they're targeting amyloid, these might become more common. And things like tile imaging may become, as well, more common. This is only used in research right now, but it may become available clinically if, again, we develop treatments for people with Alzheimer's disease.

So now that we have an idea about how to approach these patients, let's look at some clinical cases. So the first case that I'm going to show you is a person that was 81 years of age. Onset of symptoms was he one year before they presented to the clinic. We actually have neuropathological findings on all of these patients, so we know what the diagnosis was at the end. But I'm going to present the information that we gathered at the ADRC before they actually died, and before the neuropathologies told us what they had.

So he presented with memory loss, some difficulties with instrumental activities of daily living, and some-- a history of vascular risk factors. But what's important here is that when you look at those first two sentences, you realize this person has memory dysfunction and some difficulties with instrumental activities of daily living. Have they crossed that line?

Well, they have. Now they're no longer independent. If they're having difficulties with instrumental activities daily, that means someone is helping them either manage the medications, go to appointments, drive or do something else. They cannot be completely independent. That means they've crossed that line, so they're now in the dementia range.

Their neurological exam is completely normal. And on testing they have some memory alterations, some difficulties with spatial skills, but those are mild, and some mild difficulties with language. So primarily, memory is the issue. So 81-year-old, memory dysfunction, having some problems with instrumental activities of daily living, and a neuro exam that is normal.

When you look at their cognitive testing over time, what you see is that they decline, as you would expect if someone has a neurocognitive disorder. So you see they go from 23 on the MMSE to 14 at year four. So they've declined progressively.

So what do they have? Pretty straightforward, right? Since I don't have poll everywhere, you're just going to have to raise your hand. So dust this person have FTD?

MALE SPEAKER: No.

DANIEL VARON: Lewy body?

MALE SPEAKER: No.

DANIEL VARON: No. Do they have Alzheimer's disease? Anybody?

MALE SPEAKER: Maybe.

FEMALE SPEAKER: Yes.

DANIEL VARON: Maybe?

FEMALE SPEAKER: Yes.

DANIEL VARON: Who thinks this person has Alzheimer's disease? I think they have Alzheimer's disease. OK. We'll have some people-- the rest are non-believers. Vascular disease, anybody? Vascular disease, OK.

FEMALE SPEAKER: Mix.

DANIEL VARON: Mix, there you go. OK. Well, the neuro pathologies agrees with some of us, Alzheimer disease, but agrees with most of you. I think people were hesitant because you think, well, could these be mixed. Well, it turns out, yes, this could be mixed. So this person has also Lewy bodies in the neocortex. That means this was influencing in the presentation.

So you can make a diagnosis of dementia with Lewy bodies. They also have hippocampal sclerosis, TDP-43 pathology, which can be became kind of ominous, and actually potentially eight the action of these other conditions that they have. So that's actually a bad marker. And something that pathologists don't know what to do with but they report it, which is [INAUDIBLE]. They just see it. They're not sure how that plays a role into the cognitive dysfunction, and then cerebrovascular disease.

So we're thinking this person looks like they have typical Alzheimer's disease. But then, when you look at the neuropathological findings, there's a ton of things there that are explaining their cognitive dysfunction. So that's important to keep in mind. Because the older a patient is, the more likely you're going to find something like this.

So let's look at this other case to contrast with what we just saw. So this is a 67-year-old female, onset of symptoms three years before she presented to the clinic. Memory loss, word finding difficulties, some difficulties with instrumental activities of daily living, but independent for basic activities. So with those two sentences, you already know this person has crossed that line. Right? So they've gone into the dementia range. They're having difficulties with instrumental activities of daily living. Memory is the main symptom, but some word finding difficulties.

The person is a smoker and has hyperlipidemia, so there's some risk factors for vascular disease. But the neuro exam is completely normal. And on testing you find memory difficulties, visuospatial alterations that are mild, and mild language problems. So if you compare this to the previous case, it sounds exactly the same. The only difference is the age.

And when you look at it, this one progresses a little bit faster. This person, when they presented, their MMSE was 20. By the year three, they went down to 10. So they progressed a little bit faster than the previous case. And that's often what you see in the older patients. The older the patient, the slower they progress. These people that are younger, they present younger. They tend to progress a little bit faster.

So what does she have? Vascular disease? Maybe. Lewy body? No, right? FTD? Alzheimer's?

FEMALE SPEAKER: Early onset Alzheimer's

DANIEL VARON: Early onset Alzheimer's disease. She presented at 64, so probably you could say that she has Early onset Alzheimer's disease. Probably, she had symptoms even before that. So Alzheimer's disease is what the neuropathology says, and then some cerebrovascular disease, and that's it. And so when you compare these two patients, they present very similarly. The clinical presentation is very similar. The neuropathological findings are very different.

So think of that when you see patients that are older, especially if they're over 85. It's very unlikely they have just one condition explaining their neurocognitive disorder. They probably have a multitude of things. Most of them you cannot diagnose. So just keep that in mind.

So Alzheimer's disease-- if you see memory changes this of Alzheimer's disease, especially if the neuro exam is completely normal. They might have some difficulties with executive function. But language and social skills tend to be preserved for a while. They may be apathetic initially, but that's basically it. Usually their onset is in the 70s, 80s, and they are progressive a period of 10 years.

There is atypical forms of Alzheimer's disease-- posterior cortical atrophy, like I was telling you before, which is kind of usually people will have visual perception alterations. They might have difficulties with driving, grasping things, grabbing things. They see the objects, but they cannot actually grab them. And so they might go to the ophthalmologist, and they send them back to the neurologist or the geriatrician saying, no, their vision is completely fine. But what they have is posterior cortical atrophy. And you might see that on imaging.

People can present with language dysfunction, a primary progressive aphasia. And so not every person that presents with language dysfunction has a frontotemporal dementia. They can have Alzheimer's disease if they have the logopenic variant of PPA. So think of Alzheimer's disease, atypical AD, if the person presents with language dysfunction. And then this is executive syndrome. They present with just executive dysfunction. Often, that makes you think of vascular disease or frontotemporal dementia. But often those patients actually have an atypical form of Alzheimer's disease, so just think of that, as well.

Let's look at another case. So this is a 68-year-old male who presented with memory loss, were finding difficulties-- some limitations in instrumental activities of daily living, but independent for basic activities, and some motor changes. And he acts out his dreams, so he talks and punches while he's dreaming. So with that information we say, OK, well, this person has cognitive decline. They're having difficulties with instrumental activities of daily living. So we've said they've crossed that line. They now have probably mild dementia.

And you see that there are some changes in motor function, and some changes during sleep. They're apathetic. They have several risk factors for vascular disease. And their neuro exam shows some Parkinsonism. And testing shows problems in memory, visuospatial skills, but that's minimal, and some executive dysfunction and alterations in language.

So when you look at the [INAUDIBLE] person you only had two years of data, you see that they're declining, like we were saying before. So they're kind of on that downward slope. So this person has memory dysfunction, some motor difficulties, already kind of has crossed that threshold because of having instrumental activities of daily living are affected, and they're acting out their dreams. What do they have?

FEMALE SPEAKER: Lewy body dementia.

DANIEL VARON: So Lewy body dementia, right? So that's pretty straight forward. The neuropathologist tends to agree. Lewy bodies are present in the neocortex in this patient, but they also have Alzheimer's disease pathology. So you often might encounter Alzheimer's disease pathology in patients that present clinically like Lewy body, although in this case it's low level. That means that the cognitive dysfunction was primarily explained by the Lewy bodies.

They have TDP-43, as well, and the [INAUDIBLE] that we talked about before, that we're not sure what that means, and some cerebrovascular disease. So this person has several things, but most likely the Lewy bodies were kind of driving most of the cognitive dysfunction. So if you see a person that has Parkinsonism, that should come into your mind, especially if the cognitive dysfunction and the motor symptoms are close in time.

So if you have the cognitive dysfunction and soon after you develop the vasomotor symptoms or you develop the motor symptoms and soon after you develop the cognitive decline, you should think of Lewy body dementia rather than Parkinson's disease dementia. Because that's usually what happens. People with Parkinson's disease dementia usually take a while to develop the cognitive symptoms. Usually you see this-- we call it a honeymoon period, where they seem better. Their symptoms progress slowly. And then after seven years or eight years, they develop the dementia.

These people often will have some of these features, but they will not have all of them. So sometimes they'll have fluctuating cognition. Sometimes they'll have Parkinson's or sometimes they'll have visual illusions or hallucinations. And you need to ask the patient, because the families sometimes don't know about this. They don't realize the patient's having hallucinations. And you ask the patient, have you ever seen people in your house that shouldn't be there or have you ever seen children in your room when there's no one there or have you seen animals or do you ever confuse a pile of clothes for an animal or a person-- and they'll tell you, yeah, I'm seeing these things.

Sometimes they have insight, and they feel that these things are not normal they're not telling people about them. And so you need to ask them directly to see if they're experiencing any of this. REM sleep behavior disorder is really helpful because this really points in the direction of Lewy body or Parkinson's disease. So you should ask everyone, do you have these kinds of symptoms. Have you ever heard that your partner has told you this or anyone has saw you do this-- has seen you do this during your sleep?

Sometimes they fall off the bed, and that tells you that they're having some movement while they're asleep. Otherwise, you can put one of those cameras that are kind of motion activated. And that's an easy way to pick up-- like, a poor man's polysomnography. But ultimately, if you know about this, it could help you quite a bit. And this can percent earlier, and actually the patient might not have any cognitive disfunction or motor dysfunction, but this might be the only symptom you might see in some patients before they develop the neurocognitive disorder.

On testing, they usually have more visuospatial problems than memory problems, but that doesn't happen in every patient. You saw the patient that we just saw had more memory problems than visuospatial problems. So that doesn't mean that every patient is going to percent like the book says. So keep that in mind. But, in general, visuospatial problems are present.

A way to assess that is as the patient, do you ever miss the chair or has the family, do they ever miss the chair. Are they having problems with driving, parking, figuring out spaces, figuring out how far things are from their car and that sort of thing? And that can give you a sense for that. If they're having recurring falls, that's also important. Because people with Lewy body develop Parkinsonism that is not similar to the Parkinson's disease Parkinsonism.

They have more actual rigidity. Their symptoms are more symmetric. And they don't have as much tremors. See what you should check is their neck, to see if the neck is rigid. Ask them to stand up with their arms crossed in front of them, to see if they have posture instability or axial rigidity. And you can do the pull back test to see if they have some postural instability.

So the Parkinsonism might not be as evident as you would see in patients with Parkinson's disease, sometimes. They can have depression, frequently. They can have delusions along with the hallucinations. They can have auditory hallucinations, as well as visual, but visual are more prominent.

They don't have as much atrophy in the hippocampus. So if we were to look at the MRI, the MRI might look actually fairly normal, not much atrophy. And if you ask a neuropathologist, they'll tell you that often they don't find microscopic atrophy in people that have pure Lewy body disease. But if you do a PET scan, you'll have hypoactivity in the occipital regions. And that kind of reflects their difficulties with contrast perception and visual perception.

These patients tend to present in their 70s. There's a little bit higher prevalence in males versus females. And this is a very common condition. It can accompany Alzheimer's disease very frequently or it can be the other way around. People that present with Lewy body symptoms can often have Alzheimer's disease pathology. So this is a very common condition, do you have to think of it frequently.

And if you see someone that has prominent memory dysfunction that has a picture of Lewy body, and soon after that happens they start to-- I'm sorry. They have a picture of Alzheimer's disease, and soon after they start to develop other symptoms. You can always think of the two conditions being combined.

Let's look at another case. This is a patient who's 64, early onset, declined over a three year period, has language difficulties especially in fluency and naming objects, some difficulty with instrumental activities of daily living, but independent for basic activities of daily living. So, again, cognitive dysfunction primarily in language, but already some instrumental activities of daily living are affected. So they already crossed that threshold.

And they later developed some disinhibition, so the person started to be inappropriate, and they developed some poor judgment. So they started to send money out to charities and other places when they were getting things in the mail. She started to develop some specific routines. She had this routine where she had to drink tea every morning and was very rigid about it.

Her neuro exam was completely normal. And on testing she had some difficulties with visual and verbal memory. And pay attention to this-- the difficulties are pretty pronounced. So that makes you think-- I told you before, Alzheimer's disease, think of memory as the first symptom.

So this person presents with very pronounced memory dysfunction. They also have initially some-- or later in the presentation they had executive alterations. But initially, that was intact. The visuospatial skills were intact. And the other thing that they had permanent alterations in was the language, so memory and language.

This is the MMSE for this person-- initially when they presented it was 25 out of 30. And they progressed fairly quickly down to four points after four years. This is the Boston Naming Test, so they were presented 30 objects and she only could name six of them on the first visit. So she had a very pronounced language dysfunction.

Fluency initially appeared to be OK, but declined very quickly after that visit. So language and memory, like I was telling you before, were affected prominently. So this can be challenging because if you don't pay attention to the language then you focus on the memory. And patients and families will tell you always the memory is the most prominent thing. They will not talk about the language. They will not talk about the behaviors unless the behaviors are very pronounced.

So you need to kind of ask them and probe a little bit to try to figure that out. So what does she have? You could say she has a primary progressive aphasia. We would have to see the patient at two years, and determine whether or not she had any memory dysfunction at that point. Primary progressive aphasia, you need to have aphasia for two years before you develop other cognitive symptoms. This person apparently had some memory problems even before that. So you couldn't categorize her as specifically a primary progressive aphasia, but that you get the sense that aphasia was part of the presentation along with memory.

But there's also some behavioral changes. Right? So it's not clear cut. And this is usually what you see in people with front temporal dementia. They have symptoms of both language and behavior sometimes. And so it can confound the diagnosis, and especially if they have prominent memory problems. Then it makes it even harder because you start to think, could this be atypical Alzheimer's disease?

But this person had Pick's disease, so this was a front temporal dementia. Alzheimer's disease was part of the neuropathological diagnosis, but it was low level. Again, that probably didn't cause much of the dementia. It was primarily the Pick's disease that caused it. [INAUDIBLE] was present, and some cerebrovascular disease.

So when you think of frontotemporal dementia, there's two main variants-- language and behavior. Again, that can present together or they can present separately. The behavioral variant, people can present with disinhibition or prominent apathy or compulsive or very obsessive behaviors, stereotyped behaviors or dietary changes. All of those things-- if you see that early on, think of frontotemporal dementia.

If you see language dysfunction early on, think of frontotemporal dementia. So people with-- the other variant is people that have declining in language. And it could be semantic or non-fluent and grammatical. But you're not going to be able to determine that. All you know is that the person is starting to have language dysfunction. If you want to figure out what type of aphasia they have, you sent him to the neuropsychologist and they'll do a thorough evaluation. They'll tell you, this is what I think the patient has.

If they have a language dysfunction, you definitely need to send them to the neuropsychologist. Because they might come back and tell you, this looks like logopenic primary progressive aphasia, not semantic or non-fluent. And that could signify that the person has Alzheimer's disease rather than front temporal dementia. So keep that in mind.

They usually can progress fairly quickly, and they present early on. But remember, people with Alzheimer's disease can present with similar symptoms, symptoms like this, that look like from temporal dementia, both behavioral and language-based. And that sometimes can cause difficulties in terms of diagnosis.

When it comes to front temporal dementia, think of a mixed bag of things. And if you look at this graph, you can see there that, yes, front temporal dementia can present with behavioral changes. It can present with language dysfunction. But it can also present with many other things.

On one end, it can present like ALS. On the other end, it can percent like PSP. So you see this patient looks like PSP, all the symptoms that you've learned about PSP-- eye movement limitations, recurrent falls, Parkinsonism. And you say, this is PSP clinically. And then the neuropathology tells you no, it's actually front temporal dementia. So all you can do is diagnose it clinically. Don't worry about the neuropathological findings. Because ultimately, that cannot be done.

One thing that can help you figure it out is doing a PET scan or a SPECT scan. Because that will show the deficits in specific areas of frontal and temporal. But clinically it's very difficult sometimes to distinguish these patients. The opposite can also happen. People with PSP can present like frontotemporal dementia.

So when you take the basic behavioral variant, it looks exactly like a FTD with behavioral variant. And they go to autopsy, and the neuropathology shows they have PSP. So that can also happen. So just keep in mind that FTD is a mixed bag of conditions.

This is the last case I'm going to show you. This is a patient with-- a lawyer who had vascular disease, and basically presented to our clinic. The wife was the one who was noticing the difficulties. And this person was very young, was having difficulties with executive function. For the sake of time, I'm going to show you kind of the testing. He didn't do that poorly on the test, but executive function was the main problem, and processing speed.

And this is his scan, and he has prominent vascular disease in all areas of the brain, but the medial temporal regions are OK. This person had CADASIL, which is a hereditary form of vascular dementia. And it's very typical of a subcortical dementia.

These are different forms of vascular dementia. This is the one that this person would have. But in vascular dementia, the symptoms depend on where the stroke is located. So if you have a large cortical stroke, the symptoms will depend on where that stroke is located. But if you see processing speed changes, executive dysfunction, think of vascular dementia. But also think of other possible neurodegenerative disorders that could come along with that. Because that often happens. It can frequently occur with Alzheimer's disease.

And to finish, if you have someone with cognitive dysfunction and they have memory loss, think of Alzheimer's disease. If they have language or behavior, think of FTD, even if they have memory dysfunction. But keep in mind that atypical AD can happen. Do a PET or SPECT scan, and do neuropsychological testing.

If they have visuospatial deficits, Parkinsonism, visual hallucinations or fluctuations in alertness, think of DLB. But Parkinsonism can percent in other conditions, so keep that in mind. And if you have processing speed alterations, apathy or depression, think of subcortical vascular disease. But look for comorbid neurodegenerative disorders.

So with that, I'll finish. And I don't know why this happened. But I think we'll have questions at the end. All right. Thank you.

[APPLAUSE]