

# Is It Normal Aging or Mild Cognitive Impairment?

Recorded: April 2, 2025

## Transcript

### [What is mild cognitive impairment? 0:00]

*Dr. Anthony Levinson:* What is mild cognitive impairment? Mild cognitive impairment is probably best thought of as somewhere between normal aging and dementia. So they are cognitive changes that have affected the brain more than was there at baseline and more than would be expected for age. But the impairment, both the cognitive impairment, but especially the functional impairment, the impact on day-to-day, is not as severe as in dementia. So, kind of an intermediate state. Classically, or at least most commonly, the types of changes that people experience relate to memory. So, we sometimes talk about the amnesic type of mild cognitive impairment. But there are also other types of changes that may occur that Richard will talk about. And this is sometimes referred to as non-amnesic if memory impairments are not present or not the most striking change. But there is usually a subjective sense, and often family, friends, or even an assessment from a physician or an occupational therapist may note that there's actually modest impairment or changes in memory or thinking skills. So that has changed. Sometimes it can be seen on objective testing. And again, it's not severe enough to actually disrupt day-to-day life. So quite a lot of variability. So Richard, I'll hand it over to you to talk a little bit about some of the changes that might be seen.

### [Normal changes associated with aging 1:45]

*Dr. Richard Sztramko:* Sure. So, this is always a hot topic in terms of what are the natural changes associated with aging? I generally tell my patients, the brain is not different from other organs or experiences that you have. You might not be able to run as fast or jump as high, and the brain might not function exactly as it once did. So, there may be some subtle changes that occur with slower thinking speed, people may have challenges learning more complex tasks, and there may be some decline in memory, but things like vocabulary can increase over time as well as wisdom. So, the age-related changes changes do not impact independence, though. With normal aging, people will cite them as mild. Oftentimes, people might not even notice that they're taking place, and certainly loved ones or friends or the people that are surrounding the person impacted don't generally complain about the mild changes associated with aging. You can see here a picture of the brain and the various lobes within the brain itself. Different cognitive processes are localized to different areas in the brain. So, the temporal lobe, for instance, is very important for things such as memory, which Anthony just cited, but other things in terms of understanding language properly. The frontal lobe is very important for the more complex processing that we do in terms of planning, organizing, sequencing events, or

abstracting difficult concepts. It's also very important for your social functioning, understanding how to interact with the people that surround you in an appropriate fashion. So, depending on where the injury takes place and depending on what is causing the injury to the brain itself, in the case of neurodegenerative conditions like Alzheimer's disease, it may frequently impact the temporal lobe and memory first, whereas frontal temporal dementias may impact the frontal lobe first.

So, depending on where the brain is being impacted and what is impacting the brain, people will look different and have different symptoms of cognitive impairment. Here are some examples of the different cognitive domains that are associated with those various areas within the brain. So, somebody that has learning and memory dysfunction may forget medications, repeat themselves, or miss appointments. Classically, too, you may see people forget something that's happened within a day or two of an event taking place. With language, people may exhibit tip of the tongue phenomenon with problems recalling names of distant friends or acquaintances, potentially trouble expressing themselves and not finding the right words and word finding issues. With visual and spatial functions, people may have difficulties driving, initially first in unfamiliar environments and then over time in familiar environments, and they may get lost in familiar places. With respect to executive function, multitasking can be impaired, difficulty with complex decisions, and challenges with preparing meals or banking. And with respect to social function, people may exhibit changes in personality and behavior, social inappropriateness, maybe swearing at the wrong time, or unsafe decisions with money or finances.

### **[Normal aging vs. mild cognitive impairment (MCI) 5:40]**

*Dr. Richard Sztramko:* So here we'll contrast normal aging in terms of the symptoms that people may experience between normal aging and mild cognitive impairment. So, I'll use two examples from memory and executive function. So, somebody might have some mild forgetfulness, occasionally not remembering something that had taken place, or forgetting to take the garbage out, for instance. Whereas in mild cognitive impairment, people will have a consistent pattern of memory lapses that are noticed by often themselves as well as their friends and family. So, this might be forgetting their appointments or forgetting to make bill payments. With respect to executive function, people with normal aging may have some mild difficulty with complex planning or decision making. Perhaps they could whip through their taxes before, but now it's taking a bit longer. Whereas people that have mild cognitive impairment will have more consistent challenges with planning, organizing, and problem solving. And this is usually exhibited in things like finances first or cooking complex meals for large groups.

### **[Differences between MCI and dementia 6:46]**

*Dr. Richard Sztramko:* If we go further on down the chain now comparing mild cognitive impairment to dementia, you'll see the people that have dementia have significant memory loss that disrupts daily life and may include forgetting important events or people. So oftentimes at the more severe stage, people with dementia will forget things within minutes or hours, whereas that does not occur with mild cognitive impairment. And executive function, by the time you get to having a dementia, people really can't pay bills on time. They can't complete their taxes.

They can't manage any kind of accounting, and oftentimes will forget their PINS or not be able to use things like bank machines.

### **[When to be concerned about cognitive changes 7:32]**

*Dr. Richard Sztramko:* So, when should you be concerned? Repeating questions or stories in a consistent fashion, getting lost in familiar places, having significant challenges, making plans or decisions, and needing help with daily tasks are all very important red flags that people should pay attention to and make sure that they get assessed.

*Dr. Anthony Levinson:* I think one of the things too is it really does depend on the individual in terms of their background and previous education or training. So, you mentioned some of the examples of, say, people doing a more complex function like doing their taxes. If you always kind of struggled with math and that task, that might not be an indicator. But if you once worked as an accountant or your area was finance, and it's a noticeable change, others may not even notice the profound difficulty, and it may be hard to document on objective testing, but the person will also be aware of a substantial change. So often when we are doing the assessment of cognition, it's very important for us to go into the background and understand education, training, career, prior strengths, and maybe prior weaknesses before the changes had been noticed.

### **[Risk factors for mild cognitive impairment (MCI) 9:04]**

*Dr. Anthony Levinson:* So, when we talk about risk factors for mild cognitive impairment, it's quite similar to the same risk factors that we think about with respect to dementia. So we usually divide them up in terms of ones you can change and ones you can't really change. So the ones you can change, we refer to as modifiable risk factors. And again, these are quite similar in terms of the same types of modifiable risk factors that we see for dementias: physical inactivity, blood vessel health, which will come back to, hearing and vision loss, and then cognitive and social inactivity. So these are all modifiable risk factors. And within blood vessel health, high blood pressure, high cholesterol, and diabetes emerge as probably the most important vascular risk factors for mild cognitive impairment.

Non-modifiable risk factors, far and away, the biggest risk factor for MCI is age, just like it is for the dementias and the degenerative dementias, as Rich mentioned. There is also a higher prevalence of women with MCI, not just because they tend to live to an older age. Family history can play role, as can some genetics, so the same kinds of genetic risk factors for dementia. But most cases are not strongly determined by inheritance or genetics. So, there's increasing interest in the modifiable risk factors, and because it seems like there's a lot of potential to reduce the risk of MCI or maybe even prevent it.

### **[Impact of underlying diseases on cognition 11:03]**

*Dr. Anthony Levinson:* When we think about the underlying diseases that may cause MCI, on the one hand, there are all of the same diseases that may cause the degenerative dementias. So,

Alzheimer disease being the most common, but vascular disease or vascular dementia being very common. And also, the potential that there may be mixed causes, both Alzheimer disease pathology and vascular disease. So hence the focus on those reversible or modifiable blood vessel health risk factors. The other types of degenerative dementias or dementias that may be associated with MCI are things like Parkinson's disease or Lewy body disease, some of the other relatively common causes of dementia.

Potentially treatable conditions are really important aspect of the assessment and potentially reversible causes of mild cognitive impairment. And we'll talk a little bit more about that in the Q&A. But Richard and I, when we were assessing people in the hospital with cognitive impairment, we see a lot of people with medication side effects, or they have a metabolic disease, an abnormality with their thyroid gland, or kidney or liver disease, and the changes associated with that medical condition are affecting their cognition to the point where they're having signs and symptoms of mild cognitive impairment. So, part of the aspect of assessment is to rule out some of these potentially treatable conditions.

Some of the vitamin deficiencies, probably one of the more common to cause cognitive impairments would be vitamin B12 deficiency. So that's one of the ones we would often check. Sleep disorders may cause sedation and fatigue and slowed, like impairments in cognition and attention. Almost every type of substance use disorder may affect cognition. The more common ones that we see are probably alcohol use disorders. But there's many, many conditions that may affect cognition, and many of them are treatable. So, it's very important to have a full medication assessment.

### **[Progression of mild cognitive impairment over time 13:32]**

*Dr. Anthony Levinson:* When we look over time at what happens, as with many things in medicine, we say, well, you can divide it into three. Some people stay the same, some people might even improve, and some people will worsen. And so, it depends largely on the cause. So if you have mild cognitive impairment due to one of the dementias, like Alzheimer's disease, those cases are likely to progress over time. And you can see in box number three, progression is estimated to be about 5 to 15% of patients with mild cognitive impairment will develop dementia. That's the yearly risk of developing dementia. However, as you can see from that, I guess the good take home message, MCI is not inevitable, and development or progression is also not inevitable. So, some people, especially if there's an underlying medical cause that is found, their function may improve. And then those, let's say you had a vascular cause, but then you looked after all of your blood vessel health and those risk factors, you may have a very stable course of MCI. So again, not everybody will progress, but a significant number will progress, especially if the underlying cause is one of the degenerative dementias like Alzheimer disease.

### **[How to get evaluated for mild cognitive impairment (MCI) 15:15]**

*Dr. Richard Sztramko:* So, with respect to getting evaluated, the best place to start if you're experiencing any of the symptoms that we've outlined is contacting your primary care provider.

Oftentimes in your primary care provider's office, they could administer bedside pen and paper testing, where they can assess the various cognitive domains by giving a standardized test that gives a reasonable composite or global score on your general cognitive functioning. There's also the possibility then if they feel like they need additional help, they can send you to specialized memory clinics where you can be assessed by either a neurologist, a geriatrician, or a geriatric psychiatrist that might be more familiar with the various neurodegenerative types of disease or other there are more complicated conditions which could cause cognitive impairment, like seizures and the related medications that might be used in that setting.

After receiving a diagnosis and understanding where testing may lie for you, it's always useful to have annual assessments so that you can help track changes. And during these annual assessments, we will track what's been happening in your day-to-day life, functioning psychiatric symptoms that may be experiencing, repeating cognitive testing, doing physical examinations, and then reviewing various investigations that may include pictures of the brain, like an MRI or a CT scan, or various blood work.

### **[Treatment options for mild cognitive impairment (MCI) 16:09]**

*Dr. Richard Sztramko:* The question always is, are there treatments for MCI? So, am I stuck with this? What can I do about it? And within the paradigm of the improvements staying the same or getting worse, obviously, the desired outcome would be to improve things. So, it always depends on the underlying cause of the MCI itself.

So, for example, if somebody's depressed or has B12 deficiency, we can treat their depression or replete the stores of vitamin B12 using medications. The medication side effect is causing it. So, for example, oftentimes people who take medications like Ativan or benzodiazepines may be sedated and it might be causing problems. So, we can switch medications or reduce doses of medications that are causing harm. Alcohol can have acute impacts when it is in your system, but over time, it can cause damage to your brain that can stun the brain for months at a time or turn into permanent damage. So, decreasing consumption or abstaining from alcohol is very important.

With respect to toxic proteins, I'm sure we'll get into this later, there are no current treatment options for people that have MCI. There are some treatment options for people that have dementia at this time. So, if people progress and get worse, there are more treatment options. And then with respect to blood vessel damage, Anthony mentioned how important it was to prevent cognitive impairment in the first place or developing MCI. But you want to make sure that you're treating your high blood pressure, cholesterol, and diabetes so that you're not incurring strokes or the blood vessels that are in your brain are healthy. And then maintaining good general brain health with diet, exercise, social activity, and blood vessel health. So doing the things that are good for the rest of your body or generally good for your brain and can hopefully prevent any kind of further deterioration.

## **[Promoting brain health 18:54]**

*Dr. Anthony Levinson:* So Rich and I co-developed the 'Promoting Brain Health' and [dementiarisk.ca](http://dementiarisk.ca) resources. Some of you may have seen the Dementia Risk Reduction program or curriculum on the McMaster Optimal Aging Portal. We actually have also done a randomized control trial to look at the effectiveness of this education program to raise awareness about the things you can do to reduce your risk of dementia. And those same things are all things that can reduce your risk of developing MCI as well. So physical activity, weight management, blood vessel health, the importance of diet and good nutrition, smoking and alcohol are risk factors. So, if you can quit smoking and reduce or stop alcohol as well. Cognitive and social activity looks like it's increasingly important. So those people with lower levels of cognition and social activity are at higher risk for cognitive impairments. And other conditions like hearing loss, vision loss, depression, even things like air pollution have also been associated with being risk factors for dementia.

So, there's quite a lot of things that one can do. The estimates are that you can actually reduce your risk of developing dementia by about 45%. Some other studies have looked at if you can do up to five of the positive changes, protective factors or reduce risks, some studies have shown estimated reduction in cases of Alzheimer's over 50% as high as 66%

## **[Strategies to manage mild cognitive impairment 20:40]**

*Dr. Anthony Levinson:* The other strategies that are sometimes employed, and these might be used with an occupational therapist, there's some excellent programs. There's a program developed out of Baycrest that's called 'Learning the Ropes for MCI', and that is offered in person at locations around the country, I believe. I know we have some in Hamilton, and there's some in the Toronto area. They have a very good webinar that explains it. But they're big proponents of trying to use compensatory tools like an agenda, a notebook, or if you're comfortable using a smart book, to try to compensate for some of the changes that may have occurred with memory. So, using some of those strategies can help you to, if you, functionally, if you are starting to notice changes in your memory. They also have some tips for family and friends as well. Things like dosettes for keeping track of your medications, trying to look after things like sleep and avoiding stressful situations, which may also add to the cognitive load and tax. So, things like trying not to do too much multitasking and avoiding stress may also be helpful.

So again, key points, just to move in the homestretch here, a significant amount of MCI might be delayed or even prevented. It's never too early or too late to start looking at some of those modifiable risk factors. The things you do to help reduce your risk of cognitive impairment are also things that can reduce your risk of heart disease, stroke, and cancer. So what's good for the body is good for the brain and vice versa. And the more things you can address, the better in terms of modifiable risk factors.

Some of the memory and cognitive changes with aging are normal. MCI is not inevitable. And even if you do have MCI, its progression is also not inevitable. So, looking after those risk

factors, if you have a diagnosis, and using some of those other practices, like memory aids or agenda organizers, those things can help you to maintain a good function. Stay curious, stay active with your health, stay socially engaged, and that can also help you to maintain function as long as possible.

So let us now move to the many questions that came our way. So, I want to thank everybody in advance for submitting questions. And Rich, let's start off with a couple of ones that tie into the normal aging versus mild cognitive impairment.

### **[Why cognitive function varies day to day 24:00]**

*Dr. Anthony Levinson:* This question came in, some days my cognition's better than others. What causes this type of variability?

*Dr. Richard Sztramko:* I think all of us can relate to the things that can go wrong in our lives that really impact how we're feeling the next day. So, for example, my three-year-old at home has been having a sleep regression, and for the last six nights, not been sleeping quite as well. And by the sixth day, you can tell your brain's not functioning quite as well.

Similarly, you might notice that you're a little bit more dull if you've had a flu or the cold, or perhaps you have a chronic medical condition and it's not been as well controlled. Let's say you have COPD and your breathing has been really heavy, or you've taken some medications, consumed too much alcohol. There are many factors that go into your day to day life and how you're feeling generally that contribute to your health, and all of those can impact your cognition as well.

So, it's always, people are concerned about anything might happen. I always tell people it's the consistency of the symptom and the intensity of that symptom. And the more predictable it is in your life and the more frequently it's there or the larger the lapse is, then the more you should pay attention to it.

### **[Impact of COVID-19 and long COVID on cognition 25:18]**

*Dr. Anthony Levinson:* There was an interesting question that came in, and there's been quite a few people sending in live questions related to the impacts or effects of COVID and long COVID. And I think that's an interesting add on to what you were just saying. There's still, this is a very active area of interest and scientific research. Actually, I know McMaster is actually working on leading and leading an effort to create new guidelines related to long COVID, but can you say a little bit about, you talked a little bit about some of these inflammatory conditions or different medical conditions. Are you seeing folks with, say, who might be suffering from the effects of COVID or long COVID in terms of cognition?

*Dr. Richard Sztramko:* Yeah, absolutely. I would probably take one step back from that, though, too, because people think that COVID is a unique entity with respect to a viral infection causing chronic illness. And we've had chronic fatigue syndrome, which very frequently has been

enacted or caused by, we think, viral infections as well. So it's not completely new, and I know some people are a bit skeptical of it, but it's definitely an entity. We definitely see a lot of it. And we don't know how the inflammation in the brain impacts things on a permanent basis or how it impacts your endocrine function or cardiac function. But certainly there's an impact there that needs to be dealt with. And so the hard part about COVID with the lack of robust clinical trials is trying to find medications or workarounds that are off label to try and help people in the absence of very robust evidence.

*Dr. Anthony Levinson:* Yeah, we definitely see the effects in the acute hospital setting, and sometimes people with acute infection, whether with COVID or other viruses like RSV, will actually develop full on delirium and have other cognitive symptoms. And I think there can be a delay in recovery from that as well, which may look like a change if people, depending on the timing of their assessment.

*Dr. Richard Sztramko:* Yeah. And kind of like you're saying, if people have that global inflammation that changes the neurotransmitters or chemicals in their brain or changes the stress axis with their adrenal glands and cortisol, it's really a bad situation for some people to be in, and people can have impacts for many months, and sometimes people the impact it has is permanent, and we don't know exactly why.

## **[Importance of annual reassessment for MCI 28:09]**

*Dr. Anthony Levinson:* So, there's some interesting questions coming in in this other category, I guess, around understanding the progression of MCI and risk of dementia. You mentioned a little bit about getting annual reassessment.

*Dr. Richard Sztramko:* Anthony, is that you or me? So, I'll keep progressing here, and we'll wait for Anthony to try and get back on. I think he's going to be able to loop back on. His power just went out.

So, one of the questions that Anthony just brought out is the annual assessment and what we can do to establish a likelihood of somebody progressing from MCI to dementia, which is what people are worried about. So oftentimes, the test that we would rely on would be the Montreal Cognitive Assessment. And it's a pen-and-paper test. Usually, the scores for mild cognitive impairment are between 18 or 24. On that test, there are various subtests that can drill down in terms of how likely it is that the temporal lobe, which is impacted in Alzheimer's, is impacted. And if your score is below a certain threshold, it increases the likelihood of you progressing.

So, what we're really trying to find when you have MCI is the likelihood that an underlying neurodegenerative condition exists versus something that's more static. So, a good example of something that's more static is a stroke. Somebody had an incident where they had a stroke at one point in time. The damage was done to their brain, but there's no further damage that's expected to be incurred. So that person might be quite stable for a period of time. Another example is a traumatic brain injury, where somebody might have fallen off their bike, got a really bad concussion and hit their head, experienced some cognitive deterioration, but isn't



necessarily expected to have chronic progression over a period of time. That differs from somebody that has a neurodegeneration condition where they have accumulation of these toxic or bad proteins in their brain that will cause problems with the nerve cells to communicate to one another and eventually shrink and die.

So, there are a few other things that we'd note on testing. When we get an MRI or a CT scan of the brain, we can look for specific atrophy or shrinkage patterns that are associated with various diseases. So, the best example, again, is Alzheimer's disease, which is very related to episodic memory, and that's well localized to the temporal lobes and hippocampus. So, if we see that there's a lot of shrinkage in that particular area of the brain, and you're at the MCI category, then that increases the likelihood in our minds that you'll progress.

There are other biomarkers that we can look at that in Canada, we don't have as much access to. There's something called PET scanning, where we can look and actually tag the amyloid or Tau molecules in the brain and see whether they're present. That increases somebody's likelihood. If there's low levels of metabolism as well in various areas of the brain, that also will increase their likelihood of progression. So, we look at everything in totality based on the cognitive scores, the physical examination, the imaging, and the absence, really, of all of the other reversible causes. Then we can drill down and say you're more likely to progress versus less likely. And so that ties into how you reassess your MCI over time. And it's generally a combination of those things.

It's quite easy to tell if somebody is progressing, if their memory, their loved ones are discussing their care and they're talking about the symptoms they're experiencing. They can generally tell that the symptoms are getting worse in severity and frequency. So I gave the example of memory before. Somebody might have forgot an appointment every month or so, and then all of a sudden they start forgetting or missing appointments once a week, and then they're forgetting what's taking place within an hour of you telling them something or experiencing an event. So that's helpful to track. It's the symptoms over time.

And then we'll also watch the scores on the cognitive testing diminish. So, somebody might start out at a 24 out of 30 total on their MoCA. A few years later, they're down at 20 and then down at 18. And the symptoms and signs and cognitive testing generally follow one another. So, it's a bit easier to see how those things are going.

### **[Advances and challenges in biomarker research 33:50]**

*Dr. Anthony Levinson:* We had a couple of interesting questions, and I apologize. I've been living the dream of the power outage and then signing back in. So honest, I was attentively listening the whole time. But yes, I think I'm back right now. But there was a very good question talking about what is the state in Canada now around some of these other biomarkers? And I think that person may have been alluding to there's been more research coming out lately showing early changes in brains related to some of the degenerative diseases when people are testing with biomarkers or more detailed imaging and following patients for longer, that some of the pathology or brain changes or disease markers may be present 20, 30 years prior to the development of symptoms. So, this notion of pre-symptomatic disease for people with MCI

who may go on to develop dementia is very hard to diagnose in the normal way right now, because those studies were done as part of research. But what's interesting is there are also a lot of people in older age demonstrating multiple different pathologies, like those disease markers, who do not necessarily go on to develop MCI or dementia. So, a lot of the work being done now in terms of still on a research basis is trying to pull all those things together, often using machine learning or AI algorithms to say, look, can we take all of this different information, pull it together, and have a better model of predicting risk, understanding who's going to potentially develop MCI or dementia. And that may become a more reliable way in the future of determining who would benefit the most from, say, an early intervention or a treatment.

*Dr. Richard Sztramko:* Yeah. They are reviewing the Alzheimer's disease diagnostic criteria, and have really switched from a clinical assessment like, oh, your language and memory and visual spatial problems are there. And that generally is what Alzheimer's people look like, knowing that there are many different presentations, like four or five different presentations, to now moving to a pathology-based diagnosis saying, now that I can do a spinal tap and see what the ratio of amyloid to Tau is, and I can scan your brain and see that you have amyloid in your brain, it's much easier to treat that as a biologic entity in itself, as opposed to how those entities manifest in a very heterogeneous manner on the clinical spectrum. So, I think that'll be a lot more helpful over time.

*Dr. Anthony Levinson:* So yeah, so you referred to earlier the toxic proteins, and most of those degenerative forms of dementia, say, other than vascular dementia, so the diseases like Alzheimer's disease, like Parkinson's disease, like Lewy body, these are different forms of proteinopathies that, as you said, it might be important to create subtypes. It's no longer going to be just Alzheimer's disease. It'll be this is a Tau protein version or a Tauopathy version of Alzheimer's disease. So, this or that specific intervention may be more targeted. I think there's improved testing now for Alpha-synuclein, which is the protein that is involved in Parkinson's disease, and its variants, and Lewy body disease. So quite a lot of advances is being made to improve the biomarkers and diagnosis. But I think it's the state of the art on the research side has not yet translated into clinical care in Canada. And I think there are challenges with respect to both access to care, but also if there are different forms of investigations or early interventions, we are short quite a lot of neurologists and geriatricians to be able to manage that.

We have a lot of really good questions from before as well as now. So, let's keep going with some of those.

### **[Cognitive side effects of medications 38:50]**

*Dr. Anthony Levinson:* In terms of medications and medication side effects, can you maybe say a little bit about what are some of the specific medications that might be particularly worrisome?

*Dr. Richard Sztramko:* Yeah. So, anything that can have an impact on your brain. So, opioids, including things like morphine, oxycodone, hydromorphone, long term fentanyl patches, those all have quite substantial impacts on the brain. Things like benzodiazepines. So, I had mentioned Ativan or lorazepam before, Valium or diazepam, oxazepam, any of the PAM

medications often used for anxiety or to help people sleep are quite addictive and can have severe impacts. Anti-seizure medications, so levetiracetam.

*Dr. Anthony Levinson:* That's Keppra for you and me. But yeah, for sure, like valproic acid or Epival, Tangretol, almost every anti-epileptic medicine can affect the cognition.

*Dr. Richard Sztramko:* Antidepressants to a lesser degree, but when you're looking at tricyclic antidepressants in particular because of the anticholinergic impacts that they can have.

*Dr. Anthony Levinson:* Let's just pause and explain anticholinergic, because this has come up on a couple of our webinars previously. So, there's the cholinergic system is, there's a neurotransmitter, and it's very important for memory. And many, many common over-the-counter medicines, as well as prescription medicines, actually have the effect of blocking acetylcholine. So, we refer to those as anticholinergic. It's usually a side effect. Sometimes it is the target of a drug when you're trying to, say, improve bladder function. But for many medicines, including things like Gravol, Nytol, some of the older class of antidepressants, like Elavil or amitriptyline, still used quite often for pain syndromes or fibromyalgia, that anticholinergic side effect, which is common to a lot of medicines, especially psychiatric medicines, can really impair cognition so that people can definitely look like they have mild cognitive impairment or even dementia.

*Dr. Richard Sztramko:* It is interesting, too, when people are like, the other side effects are having dry eyes or dry mouth or not being able to go to the may not be able to urinate freely. And the amount of people that come in and will have substantial side effects after being on these medications for a long period of time and then have it also impact the cognition with the cholinergic system in the brain is quite interesting.

Other medications, so like gabapentin or pregabalin, are also quite commonly used for chronic pain related to nerve conditions, and they can cause confusion, sedation as well as problems with coordination. So oftentimes, you want to get people off of the medications for the primary reason of cognition, because that's how they present. But these medications are also associated with sometimes poor sleep, with falls, with daytime sleepiness. So, there's a lot of other benefits that people get from getting off these medications. Antipsychotics would be another realm, risperidone, quetiapine, loxapine. There's many, many others, but that's just to name a few more commonly used ones.

*Dr. Anthony Levinson:* It was a good question about, can surgery, pneumonia, or illness cause memory loss, and will it recover? And we have talked previously, and we have an e-learning lesson about delirium or acute confusion that is often associated with a serious medical illness. And it's important to realize that while many, many cases of delirium are reversible, so if you identify and treat the pneumonia or the major illness, or you recover from the surgery, for some people, it can take quite a long time, and so they may have a longer period, even after they're discharged from hospital, where they are noticing memory impairments. And I think it's something like 80% of patients, especially if they're vulnerable and they've had a severe episode of delirium, they may still have symptoms of delirium for some time.

## [Vitamin B12 deficiency and cognitive impairment 43:51]

*Dr. Anthony Levison:* We have a question about vitamin B12. How can you tell if you have a B12 deficiency and what's the best way to improve it? Should all seniors take a B12 supplement?

*Dr. Richard Sztramko:* B12 can be a bit challenging. So, if you have severe B12 deficiency, you can get something called a megaloblastic anemia, where there's something, your cells get a little bit large. You'll get abnormalities to your white blood cells. That's honestly if you have very severe deficiency. You can get neurologic damage to your peripheral nerve. So people sometimes get numbness or tingling. They can also get damage to their spinal cord. But these are really on the severe continuum of disease, and oftentimes people can have more mild effects with lower levels.

So, the best way is to just get a level checked. Generally, if it's above 300 in Canada, you don't really have to worry about it. If it's between 200 and 300, you may require additional testing. Often, I'll send people for a homocysteine level just to see if that's abnormal because you can still will be deficient technically at the cellular level, even though your levels are normal. And then if you're below 200, then it's a much higher probability. It's not a bad thing if people are generally below 300, then we'll treat. It's not a high-quality scientific recommendation, but you don't want to miss that window and have people fall too low and then run into the more severe, significant problem.

*Dr. Anthony Levinson:* Yeah. It actually will, if it's untreated, can affect the white matter in the brain, and can be associated as one of the potentially reversible causes of cognitive impairment, can also be associated with depressive symptoms and anxiety, and if caught in time and treated appropriately, all of those neuropsychiatric and cognitive symptoms may improve. But a lot of the original levels that were determined about what was a healthy level were actually based on people having more severe problems like anemia, and they weren't necessarily looking for more subtle cognitive or psychiatric symptoms. So good idea to get it checked and know one way or the other. The most common cause of B12 deficiency seems to be more age-related. It's actually hard to extract the vitamin from food as we age. We don't produce acids the same way. So people who are on medications for stomach acid, like reflux, they are at slightly higher risk of developing B12 deficiency as well, or if you've had a surgery to your small intestine.

*Dr. Richard Sztramko:* The nice thing, I think, with B12 is that we used to figure you have to have injections, but now, if you get a super physiologic dose and get a lot into your small intestines, you can still absorb enough of it, which is good.

I do want to caution people, though, because it's really important to get the reversible causes addressed and ruled out, which we can do quite quickly, but trying to temper people's expectations and that the large majority of people don't have any reversible causes. Maybe your B12 is a bit low. We'll treat your B12 level, but it doesn't often make a big difference to most people that are presenting. So, it's important to rule out, but the majority of people are in a different paradigm with not easy to reverse conditions.

*Dr. Anthony Levinson:* Probably the most common reversible things that I would see would be medication side effects. So really going over your medications with a pharmacist and with your physician to say, hey, is there any of these that could be causing problems? Do I need them all? What are the most likely ones? That would probably be the most common along with alcohol.

*Dr. Richard Sztramko:* You know what might be interesting these days is just if you have access, typing all your medications into ChatGPT and say, hey, let me know if I've got some interactions and any cognitive side effects and flag them and take them to your pharmacist or doctor.

## **[Addressing denial about cognitive decline 48:01]**

*Dr. Anthony Levinson:* Yeah. So, I want to cover a few other key topics here. What do you do with a friend or spouse who refuses to acknowledge cognitive decline? We had a few of those. What to do with a spouse or a partner is in denial about MCI.

*Dr. Richard Sztramko:* Yeah. I mean, being loving and kind and just continuing to support them because there's not a lot you can do until they're very, very severe and have gone down the path of having dementia and are no longer capable. So, the first thing is just being kind and being consistent in your feedback, but not overwhelming people. And then trying to get them, however you can, to a professional that has a certain demeanor, that has a familiarity, that doesn't have to be severe or awkward in how they're dealing with the topic.

I think a lot of practitioners aren't comfortable in dealing with this issue. And so, if you have comfort and you're confident in your diagnosis, you can be a little bit more laid back and approachable. And so, I think that's the important thing is getting people to a trusted professional that can guide them through that, not being too heavy-handed because that will just push people away. And then what I found is helpful sometimes is people actually documenting and taking it to people in a kind way. Like subjectively we always have arguments like, Oh, did this happen? Did it not happen? But if you actually documented like, Hey, well, you forgot this, and this was a big issue for our family, and you missed this bill payment, and these are things that we've noticed over time, and build your case, then sometimes people can be more agreeable. I'm not sure, do you have any additional suggestions, Anthony?

*Dr. Anthony Levinson:* I think it's one of the more challenging aspects of it. I want to say it's also a very common one. I like the way you phrased it, and I can still imagine somebody who's like, 'Why are you all coming at me? 'Why are you attacking me?', because I just think it's very challenging. And there may also be some emotional or executive changes that make the person a little bit more irritable, or less accepting of it, or a little bit more, yeah, a lower frustration tolerance. So that if somebody with good intentions is coming, to suggest you get an assessment, it could be more challenging than it might have been otherwise. So, we do see with some people, basically, emotional and behavioral changes related to the mild cognitive impairment. So, they can become more emotional or irritable, more changeable or labile in their mood.

*Dr. Richard Sztramko:* And the concept of insight, right? Is like some people are like, wow, I really know that I have a problem, and other people are completely unaware of the problems that they have. So, getting the testing done, too. If you can actually show somebody like, Hey, this was a pretty easy test, and this is how you did on it. You missed this clock drawing and your cube was not very good. So, this is just something we have to work with. You're not attacking, but you're just providing information that's more objective to them.

*Dr. Anthony Levinson:* We've had a couple of other questions, and I do want to respect everybody's time and wrap up soon. So, we'll maybe hit three more items that have come in.

## **[Sleep disorders and cognitive impairment 51:52]**

*Dr. Anthony Levinson:* A few questions on sleep. What exactly is a sleep disorder? And is poor sleep a cause of MCI?

*Dr. Richard Sztramko:* Yeah, so definitely poor sleep can contribute to poor cognitive testing. Sleep disorders can be quite broad. So, they can be something like obstructive sleep apnea, which could have an anatomic component in people that are quite obese, and it causes you to stop breathing in the middle of the night, causing poor oxygen flow to the brain and cognitive impairment in that fashion, with daytime sleepiness and a propensity to fall asleep. And if you get treatment through CPAP or BiPAP, which are those masks that people wear overnight, then that causes people to be able to breathe and get oxygen in their brain overnight and overcome the illness there. So that's an example of a sleep, sleep disordered breathing that can really profoundly impact your cognition. Anecdotally, I've seen people have no other causes, get diagnosed with sleep apnea, start CPAP therapy, and their cognitive testing can improve between four and six points and give them energy and all of that stuff. So, temper people's expectations, but that's a possibility.

There are other sleep disorders, such as restless legs, where people may have iron deficiency or be on medications which can cause it. But it causes your legs to have an abnormal sensation, and when you move them, it can go away. So that can keep people up. Another example would be a periodic limb movements of sleep where your legs just move on their own. We don't know why precisely. And I'm not a sleep expert. There are sleep experts. But that keeps your brain from going through the normal patterns and stages of sleep, which caused sleep to be restorative. So, anything that impacts you from a primary sleep disorder point of view can impact your cognition the next day.

Now, there are more theories in terms of the beta-amyloid protein in the CSF gets cycled, it gets stored in your brain and into your CSF. And a lot of that replenishing and clearing of the amyloid from your brain seems to happen in sleep. There are animal models of mice that have been sleep-deprived that will accumulate more amyloid protein than if they weren't sleep-deprived. So not only does it impact your ability to just function immediately because your brain needs sleep, but it's also theorized that chronic sleep deprivation may worsen the accumulation of the toxic proteins that can cause Alzheimer's disease. So, there's a lot of reasons to do that sleep hygiene thing and try and get the most sleep you can.

*Dr. Anthony Levinson:* We did, with Dr. Sophiya Benjamin, we did a talk on sleep disorders and more focused on insomnia and treatments for insomnia. So, we can also send out a link to that talk in the follow-up email. One other condition, there's a specific type of sleep disorder called REM sleep behaviour disorder that is associated with Lewy body dementia in particular. So that's not necessarily causal in terms of the poor sleep impacting cognition, but there's definitely an association between sleep disorders and cognitive disorders as well.

*Dr. Richard Sztramko:* I mean, that's an interesting one with the Parkinson's and DLB and multi-system atrophy. So if people have just REM sleep disorder and you follow them for five years, it's like 30% of people will develop Parkinsonian syndrome. And if you follow them for 10 years, 70 to 80% of people will develop it. So, there's something intricately tied between REM sleep disorder and the alpha-synucleinopathies.

*Dr. Anthony Levinson:* And we'll also in the follow-up, we'll be sharing the handout with some other resources as well as the sleep disorders.

### **[Long-term use of antidepressants and risk of MCI or dementia 56:11]**

*Dr. Anthony Levinson:* A couple more questions before we wrap here, but there was a question or a few questions around long term use of antidepressants, particularly the most common type, SSRIs, or selective serotonin reuptake inhibitors, and can they contribute to MCI or dementia. I will say at this time, there is no evidence of SSRIs and a strong association with MCI or dementia. And I will say there is an association with depression as a risk factor. So, the best thing in terms of dementia risk reduction or MCI risk reduction would be having treatment for depression. That could be non-pharmacologic treatment, but it may also involve medications like SSRIs.

There are a couple of the SSRIs that do have that anticholinergic side effect we were talking about earlier. One of the ones that is probably the most anticholinergic is paroxetine or Paxil. So, if you're having cognitive side effects, and you're on Paxil, that might be a good to ask your doctor or pharmacist if they think it could be contributing, but not so much as a risk factor, long-term use has not really been strongly associated with MCI or dementia.

### **[Concussions and increased risk for MCI or dementia 57:48]**

*Dr. Anthony Levinson:* One final question, and then I just want to highlight a couple of things. So, any research that you know of on concussions at an early age due to sports, and then maybe again in later life, that might put people at increased risk?

*Dr. Richard Sztramko:* Yeah. So, in early life, if you have a traumatic brain injury associated with loss of consciousness, it's one of those things that increases your risk. But not dissimilar to smoking or high blood cholesterol or the other lifestyle factors that you had mentioned. So, it's not something where it's causative. It's just something that's interesting to know.

Certainly, in people that have recurring current traumatic brain injury, whether that's more overt or repetitive in the form of athletic endeavours. So, people that were enforcers in hockey and had head trauma related to fighting. Or linemen or linebackers in the NFL can be prone to something called chronic traumatic encephalopathy, which is its own pathological entity and has its own various symptoms. But that's a much more severe form compared with somebody saying, I fell off my bike when I was 10 and I had a bit of a concussion. It doesn't really mean that much, to be honest.

*Dr. Anthony Levinson:* It's really, I think it will be an active area. Most of the literature talking about cognitive impairment is due to a traumatic brain injury, and that traumatic brain injury is generally defined as having been severe enough to have led to a loss of consciousness. I think with understanding the impact on athletes' brains that's emerged over the last couple of decades and increased understanding to some degree about concussions, I think there'll be a little bit more research to maybe better understand longer term impacts of concussion.

*Dr. Richard Sztramko:* Now, there is some basic science research that suggests that a profound injury can set yourself up for secondary development of a neurodegenerative condition. An autopsy reports of people that have been in car accidents, they do see some secondary beta-amyloid, like Alzheimer's, in people that are even younger. So, there is a possibility there, but nothing, again, that we can be certain of or quantify in terms of.

*Dr. Anthony Levinson:* Yeah, I think the theory, too, conceptually, that you may have a bit of a vulnerability from childhood injury or concussions, and then it, in some ways, may lower your threshold for later injury in later life to increase your vulnerability. I think that model makes sense and also highlights, again, the importance of engaging in protective factors and risk reduction, because I think if you think about that balance between risk and protection, if you had head injury, concussion in your younger years, then do what you can to optimize the protective factors.

*Dr. Richard Sztramko:* Yeah, the cognitive reserve.

*Dr. Anthony Levinson:* Exactly. Yeah. So, I'll thank Richard again at the end, but just a note for those of you who are less familiar, though, the McMaster Optimal Aging Portal is a free resource. You'll notice there's a large red donate button at the top of the interface that helps to enable us to keep it free. So, I want to thank people who have donated over the last few years, which has made it possible for us to continue doing webinars, as well as offering the great resource of the evidence-based content that composes the McMaster Optimal Aging Portal.

There is a free weekly email newsletter Maybe some of you heard about our e-learning resources or evidence-based blog posts, evidence summaries or webinars through that. It's a great way to keep atune to new evidence-based content that comes out on the Portal weekly.

We do record these videos. The Alumni Association does as well. Christine is going to send the follow-up email for that. We also host videos on the Portal as well. And you can access e-learning related to dementia risk reduction, mild cognitive impairment, there's a new dementia series based on the work that Richard and I have done with the iGeriCare resource for care



partners of people living with dementia. And those usually have the e-learning lessons are often accompanied by micro-learning. So, these are shorter weekly emails. Some of them are three weeks, four weeks, up to twelve weeks, that summarize some of the content from the special e-learning series as well. We also have a YouTube channel. So, the insomnia and sleep disorders recorded webinar is available through the Portal. It can also be accessed there.

**DISCLAIMER:** The information in this video was accurate as of the upload date, 04/02/2025. This transcript has been provided for informational purposes only. They are not a substitute for advice from your own health care professional. This transcript may be reproduced for not-for-profit educational purposes only. Any other uses must be approved by the McMaster Optimal Aging Portal ([info@mcmasteroptimalaging.org](mailto:info@mcmasteroptimalaging.org)).