



A PODCAST  
BY PHYSICIANS  
FOR PHYSICIANS

HOSTED BY DR. DAVID GRATZER

April 26, 2023

## The big sleep update with Dr. Michael Mak

[Musical intro]

Running time: 15:39

**David Gratzer:** I can't sleep. The last time a patient told me that was about two seconds ago. As clinicians, we often hear patients complain about sleep, about the length of sleep, the quality of sleep, and that's not surprising. Sleep can be disturbed by mental disorders, by problems unrelated to mental disorders like pain. And of course, our patients respond to stress just like you do, and I do. Sleep. New medications. New therapies. What to make of it all?

Welcome to *Quick Takes*. My name is Dr. David Gratzer. I'm a psychiatrist here at CAMH. Joining me today is Dr. Michael Mak, a psychiatrist at CAMH. Dr. Mak's academic interests include sleep disorders and psychiatric patients. He is an award-winning educator and serves on the education committees of both the Canadian Psychiatric Association and the American Academy of Sleep Medicine. And he's creating a fellowship on sleep right here in Toronto. Welcome, Dr. Mak.

**Michael Mak:** Thank you, David.

**David Gratzer:** Now, you are a general psychiatrist with a strong interest in sleep. Are you a sleep psychiatrist with a strong interest in general psychiatry?

**Michael Mak:** You know what, I'm both. Like the lines between sleep, health and mental health in general are blurred. We know that almost all psychiatric conditions have some sleep component to them. And of course, we have specific disorders where sleep is enshrined in the diagnostic criteria. Things like major depressive disorder, generalised anxiety disorder and of course post-traumatic stress disorder. But the vast majority of folks with sleep issues will have mental health challenges and vice versa.

**David Gratzer:** You have inpatient beds here at the Centre for Addiction and Mental Health. What are some of the most common sleep complaints that you hear day to day?

**Michael Mak:** Well, the most common one would be insomnia. Symptoms: problems falling asleep or staying asleep. We know that in patients with mental health conditions that there is comorbidity of about 80%. You know, folks with either depression or anxiety, bipolar mania, schizophrenia, these are folks that have a lot of issues, problems falling asleep and staying asleep.

**David Gratzer:** These problems are enormously common. Comorbidities are high, as you suggest, though most of us haven't done so much extra in terms of training around sleep, which makes you a bit unique. How did you get interested in this topic?

**Michael Mak:** Well, I was lucky to have done rotations with folks involved in sleep medicine in a variety of different disciplines. Folks that practice sleep medicine can be psychiatrists, they can be neurologists and respirologist (lung doctors). And you know, as a student, I had the luxury of rotating through all those disciplines as they interact with sleep medicine. But personally, I was most interested and fascinated about the mind. You know, in psychiatry we have a background in dream analysis. So a lot of the folks that are involved with sleep medicine at the beginning of sleep medicine and its birth were psychiatrists. And that's how I got involved.

**David Gratzer:** We've got a rich history of sleep and sleep medicine in in the Toronto area, no?

**Michael Mak:** Absolutely. You know, in particular in our Department of Psychiatry and the University of Toronto, there's been a number of discoveries that have been made. So first off, recognising that Dr. Harvey Moldofsky, who is probably the person to open the first sleep lab in Ontario at the old Clark [Institute of Psychiatry], he had a three-bed lab there beginning in the early '80s. And you know, one discovery that he made that stands out is the association of what we call alpha delta sleep and patients with pain disorders like fibromyalgia. So Dr. Moldofsky was one of the authors, co-author for the first set of criteria for fibromyalgia. So for us, when we're awake, but with our eyes closed, the brainwave that predominates is alpha, alpha waves. What he found was in deep sleep or slow wave sleep, when usually the brain is at its greatest level of rest, there is a superimposition of alpha sleep on top of the delta waves. And what that demonstrates is that in folks with untreated pain disorders and fibromyalgia, that the brain reflects a state of trying to rest, but also having this wakefulness because the alpha waves are reflective of a person that's awake with their eyes closed. It's a biological correlate of something that at that time was thought to be maybe just psychological.

**David Gratzer:** Is there anyone else who is deserving of mention when we talk about sleep and the University of Toronto?

**Michael Mak:** There's a psychiatrist, Dr. Mortimer Mamelak. I think he's significant in the sense that he was the person who opened the first sleep lab at Sunnybrook Hospital, a two-bed lab in the early '80s. He's a psychiatrist with a large department, and he pioneered the discovery of sodium oxybate as a treatment for narcolepsy. Up until that point, there were no reliable treatments for patients with narcolepsy. But he discovered that sodium oxybate given at bedtime will treat narcolepsy well. And patients all around the world travelled to Toronto to see him to receive this pioneering treatment.

**David Gratzer:** Let's pivot to perhaps clinical scenarios a little bit more relevant to our listeners. So thinking through the different sleep disorders, insomnia is probably the most common, maybe the most debilitating, though certainly there are many sleep disorders out there. There's been huge shifts in terms of the psychopharmacology and also the therapies available. Why don't we start with psychopharmacology. How have things evolved over time?

**Michael Mak:** Well, when we think about historic treatments for insomnia, things like barbiturates, benzodiazepines and z-drugs, even though they worked well, they all carried significant side effects, things like addiction and tolerance. So if a person was taking them for a prolonged period of time, their bodies would get used to these substances and it'd be hard for them to come off of them. Sometimes patients would be stuck on them for many years, and if they tried to stop taking these medications, they would get rebound, insomnia. Their sleep would be even worse than what it was before they came in for treatment. We also know that there's adverse effects as it pertains to causing problems with memory and concentration. Next day grogginess, brain fog. And we know that impairs balance in patients, especially those who are 65 and above. You know, when we study these medications and the elderly, we know that there's a significant risk of falls that lead to hip fractures and then lead to increased rate of death. So we had treatments, they worked well, but they were all limited by the potential adverse effects.

**David Gratzer:** Lots of problems with the old meds. What's new?

**Michael Mak:** In terms of new treatments for insomnia disorder this is sort of an exciting time. We have a whole new family of insomnia treatments. They're called dual orexin receptor antagonists. You're aware that there's a sleep disorder called narcolepsy and in this condition patients with narcolepsy are irresistibly sleepy. That is the hallmark symptom of that condition. They're sleepy all the time and it's unquenchable. So when we study these patients, we know that they have a deficit of a neurotransmitter called orexin. And it transpires that orexin is the main neurotransmitter that promotes alertness during the daytime for all folks. So chemists came up with the idea of blocking that transmitter and its receptor to see if it would induce sleepiness. And it transpires that it does. It induces sleepiness in the patients where we block this receptor. So we have medications that have this exact mechanism and it shows great promise because in comparison to older treatments, the side effects seem to be far more tolerable. So there's a less risk of addiction and tolerance, but also it doesn't seem to have that impairment to cognition the next day. So less brain fog the next day. And it doesn't seem to impair balance like the older drugs do. So it's a very exciting time.

**David Gratzer:** Do you think this class will eventually replace some of its older cousins?

**Michael Mak:** I think time will tell, but for the time being, based on the data that we have, it seems like it will because it shows equal effect. It's equally as effective, but it's much, much more tolerable.

**David Gratzer:** So this is something you've started to prescribe?

**Michael Mak:** Yes, I have.

**David Gratzer:** And if they had trouble with insomnia, if we were to use generic names, what medication would you pick of this new class?

**Michael Mak:** Well, what's available now is something called lemborexant. It's the first fully available version of this family of medications, and I suspect that other ones will follow.

**David Gratzer:** And how do you prescribe?

**Michael Mak:** You would prescribe lemborexant at 5 to 10 milligrams at bedtime. So we advise patients to try five milligrams first for seven days. And, if after a week there's still room for improvement, you can try two tablets. So ten milligrams at bedtime. We advise patients to give themselves at least seven hours a night in bed after administration. In terms of potential side effects, it can cause headache, vivid dreams and sleep paralysis.

**David Gratzer:** We've talked about meds. What about therapies?

**Michael Mak:** Yeah. I mean, at the end of the day, the best treatment for insomnia is not medications, it's therapy, namely cognitive behavioural therapy for insomnia. And the reason why that's the best treatment is because it's been shown to be equally as effective as any sleeping pill in existence. Secondly, the gains are durable, meaning that when people complete the course of cognitive behavioural therapy for insomnia, the symptoms tend not to return.

**David Gratzer:** And of course we've got newer forms of CBT in way of apps and online applications. What are your thoughts?

**Michael Mak:** Well, traditionally the challenge about CBT-i is access, and I think that that falls with other forms of therapy, right? So, you know, we'd like to have all insomnia patients be able to receive cognitive behavioural therapy for insomnia, but the supply of this highly demanded resource is actually very small. So we foresee that technology and electronic versions of these therapies as a way to bridge that gap, that gap of access.

**David Gratzer:** Do you have an app that you particularly like?

**Michael Mak:** Well, I want to put a plug for something that we've been doing in terms of research. So one of our residents in the program, Arvind Rukmani, he's writing a scoping review of validated cognitive behavioural therapy for insomnia applications on smartphones, in collaboration with Colleen Carney, who's a professor of psychology at the Toronto Metropolitan University, who is sort of a thought leader in insomnia treatments. And he's identified five apps that are validated by literature. So Sleepio CBT-i Coach, Sleepate, Sleep Ninja and Somryst, but maybe the one that's easiest to access because it's free would be CBT-i Coach.

**David Gratzer:** A patient comes to you complaining of insomnia perhaps in the context of depression doesn't have the financial ability to pay for private therapists. Is that your go to app?

**Michael Mak:** Yes.

**David Gratzer:** We've talked about insomnia. Let's pivot for a moment on a newer sleep disorder, a newly recognised sleep disorder, REM behavioural sleep disorder. Tell us about it.

**Michael Mak:** Yeah. This is a condition where a patient will act out their dreams. And this is in contradistinction with non-REM parasomnias. These are things that we're very familiar with, especially if you've been a parent. You know, we know that young folks have a tendency to develop non-REM parasomnias they might do sleep walking or have night terrors, and that affects up to a third of younger folks. REM sleep behaviour disorder affects older folks, disproportionately males. In these patients, they act out their dreams. So if they're dreaming about playing baseball, they're going to start trying to hit the ball with the bat, even though their eyes are closed and the patient is asleep. What's interesting about this condition is that it is sort of the canary in the coal mine for the development of neurological illness later on in life. So we know that in patients that act out their dreams on a regular basis that they will later on in life likely develop an alpha-synuclein apathy. Things like Parkinson's disease, multiple system atrophy and Lewy body dementia. So, you know, what's interesting about this condition is that because we know the average time it takes for a person to develop those neurological conditions after they start acting out their dreams, there's a period of about ten years and now this is a window for us to try treatments that affect the prognosis and the course of these conditions. Maybe this is the time that we can find out if there's a medication that can prevent the onset of Parkinson's disease.

**David Gratzer:** It is a tradition of *Quick Takes* that we finish with a rapid-fire minute. Are you ready?

**Michael Mak:** Yes, sir.

**David Gratzer:** Are you awake? Okay, let's put it a minute on the clock. Here we go. Dr. Mak, what's the biggest change you've seen over your career with regard to sleep?

**Michael Mak:** Tools that we have in terms of diagnosing sleep disorders. I think that there's going to be a trickle down from research level technology, things like actigraphy, which is a measurement of movement. And we'd like to think that, you know, an absence of movement is associated with sleep. We know that the more advanced forms of this technology that were used in research are slowly trickling down to consumer based, consumer grade level fitness trackers. And that's going to open the door for mass diagnosis, maybe better treatments for patients.

**David Gratzer:** Do your patients use apps?

**Michael Mak:** Absolutely. A lot. A lot of them will come in with outputs from their sleep trackers, things like the iWatch or Fitbit and Garmin. And those do a pretty good job of telling us when a person falls asleep and wakes up and how long it takes for them to do so.

**David Gratzer:** And at the buzzer. One last question. What do you do when you can't sleep?

**Michael Mak:** What I do is that I'll do something boring until I feel my head nodding again and sleepiness. So I like to do a word search if I'm up in the middle of the night or having trouble falling asleep at the beginning of the night, and when I find myself nodding my head and feeling that natural wave of sleepiness, that's when I go back into the bedroom.

**David Gratzer:** Sleep is an important topic. We appreciate the update, and we appreciate your time.

**Michael Mak:** Thank you so much.

**David Gratzer:** Thank you, sir.

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