



INTERVIEW SPOTLIGHT

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Clearing The Smoke On Cannabis

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DR. JAMES MACKILLOP IS A PROFESSOR OF PSYCHIATRY & BEHAVIOURAL NEUROSCIENCE AT MCMASTER UNIVERSITY, THE DIRECTOR OF THE PETER BORIS CENTER FOR ADDICTIONS RESEARCH, AND A CO-DIRECTOR OF THE MICHAEL G. DEGROOTE CENTRE FOR MEDICINAL CANNABIS RESEARCH. DR. MACKILLOP'S RESEARCH INTERESTS INCLUDE ADDICTIVE BEHAVIOURS SURROUNDING ALCOHOL, TOBACCO, GAMBLING, AND OBESITY. MORE RECENTLY, HE HAS BEEN INVESTIGATING BOTH THE BENEFITS AND RISKS OF MEDICINAL CANNABIS TREATMENTS FOR VARIOUS CONDITIONS.

■ HOW DID YOU GET STARTED IN THE FIELD OF ADDICTIONS RESEARCH? WHAT LED TO YOUR RESEARCH IN THE CENTRE FOR MEDICINAL CANNABIS RESEARCH (CMCR)?

It's been an evolution. I was always interested in psychology and I wanted to be a clinical psychologist, so that's what I studied in graduate school. Initially, I wasn't sure where I wanted to specialize. I worked in a laboratory doing schizophrenia research and I decided that it was not the direction I wanted to go. At the time, I was really interested in binge drinking among young adults; I was interested in studying alcohol misuse and that's what I explored in graduate school. From there, I broadened my interests to other drug and behavioral addictions, including gambling disorders and compulsive eating. Only recently have I started focusing on the other [therapeutic] side of the coin: the medical applications of cannabis, which is in the context of the new CMCR.

One of the things I love about being an addictions researcher is that it is an intersection of many different fields [such as] ... behavioral genetics, ... psychology [and] ... cognitive neuroscience. Addiction has real-world impacts in terms of healthcare delivery, crime, and the economy, so all of these different disciplines have their own perspectives on addiction. Therefore, addiction is an incredibly multidisciplinary area that allows you to look at a significant social and health

concern through a lot of different lenses. [You] gain different perspectives based on the one you choose.

■ WHAT ARE THE CURRENT PRIORITIES IN MEDICINAL CANNABIS RESEARCH?

The interesting thing about medicinal cannabis use in Canada is that there has [recently] been a skyrocketing increase in the number of people who've sought a physician authorization for medicinal cannabis. Over the last four years, we've seen close to a 3000% increase in the number of people who have sought an authorization, and I believe that number is now over 300,000 Canadians. This increase is not because the associated evidence has also skyrocketed. The reality is that the evidence hasn't changed all that much over the last couple years—that's just the nature of health research. The other reality is that specifically in the context of medicinal cannabis, the evidence is not as strong as we would like in a number of areas. Most authoritative reviews have suggested that there is moderately consistent evidence for some conditions, such as nausea in chemotherapy patients and muscle spasticity in those with multiple sclerosis. However, for a lot of other conditions, the kind of evidence that we would look for, especially gold-standard randomized control trials, haven't been conducted. This causes a real disconnect between the research being conducted and what people are actually using medicinal cannabis for. We feel like there is a real need for much more coordinated, dedicated, clinical and pre-clinical research on cannabis.

■ WHAT ARE SOME EXAMPLES OF CURRENT RESEARCH HAPPENING IN THE CMCR? WHAT OBSTACLES HINDER OUR ABILITY TO PRODUCE QUALITY RESEARCH ON MEDICINAL CANNABIS?

At the CMCR, we're supporting a variety of different pilot research initiatives. These include early stage trials looking at cannabis [treatment] for specific conditions. In other cases, it's more observational research. For example, we're conducting evaluations of patients in clinic who may be using cannabis, medically, or non-medically, to see how that interacts with their treatment prognosis. In other cases, there are laboratories investigating new therapeutic indications for cannabis and specific combinations of cannabinoids and their [associated] risks. For example, we're looking at new combinations [of cannabinoids] as possible treatments for pain but we're also looking at how cannabis smoke may have adverse consequences on lung function. We're really trying to look at the whole spectrum of research, from basic science to clinical science, to move forward in terms of knowing where the best evidence is.

Historically, one of the obstacles has been that when you are trying to study an illegal product, it's unlike studying alcohol or tobacco where there are quality assurance standards and manufacturing standards. If you tell me that you drank a Molson beer, I know how much ethanol is in that drink, so I can be fairly sure of [your intake]. If you bought some

cannabis off the street and smoked it, I don't really know what's in it. I can "guess-timate" some levels of THC [or] we could take a sample and test it, although that's actually quite challenging. It's been a more opaque world out there in terms of contraband cannabis because there are variable levels of THC and there can be other products laced in. The more general issue with cannabis is that THC, the compound people are most familiar with because of its psychoactive effect, is not the only component. There are literally hundreds of other compounds and over a hundred different endocannabinoids/phytocannabinoids, which are the plant compounds that actually act on our internal endogenous cannabinoid system. The best known is THC, but cannabidiol (CBD) is the other one people hear a lot about. Thus, in that illegal market, we have very little knowledge about what people are consuming. With legal medicinal cannabis and now legal recreational cannabis, we're going to have a much better sense for what's being consumed and what the possible consequences could be. For example, we may discover that there are more adverse consequences for individuals using THC products, or perhaps less harm for people using high CBD or lower THC:CBD ratios. The other thing is that we are going to have much better access to products that we can study. If you want to do trials or experimental research, you have to administer these substances under controlled conditions. I think that hopefully, with legalization, there will be an easier system for getting access to cannabis products in order to better study it in the laboratory and the clinic.

■ IF ANY, WHAT ARE THE MISCONCEPTIONS SURROUNDING THE USE OF MEDICINAL CANNABIS THAT PEOPLE MAY HAVE?

In my opinion, there are two families of misconceptions. There are many conditions for which people use medicinal cannabis. If you look at the Health Canada documentation, I think that there are more than 25 possible conditions listed, and if you search for medicinal cannabis use on the internet, you'll find much longer lists. Recently, I was shown a site identifying over 200 different conditions. One of the misconceptions is that just because someone says you could use medicinal cannabis to treat something then there's good evidence that it would actually be helpful, or that these lists, even from Health Canada, have the same amount of evidence from one [condition] to another. The reality is that the scientific literature is very lopsided; there are some conditions for which there is reasonably good evidence, and then there are conditions for which we have no evidence. In healthcare, you generally don't want to recommend things for which you have no evidence apart from anecdotes or observational data. [These data] are certainly clues but are not the kind that one would ever use to get approval from Health Canada or the FDA. So I think the first misconception is [the belief] that the evidence behind indications are equal.

The second misconception is that medicinal cannabis is relatively benign and is healthier and safer than other medications because it's a plant product. However, there are lots of natural things that are unsafe and unhealthy. For

example, you wouldn't encourage someone to go out and eat mushrooms that they've self-foraged. The reality is that natural does not mean safe and we should think of medicinal cannabis as any other drug. Unfortunately, for virtually all drugs used to treat medical conditions, there are benefits we are looking for —the on-target therapeutic effects— and then there are the side effects. One of the things we encourage people to realize is that there are two sides of the coin when it comes to medicinal cannabis; in some cases it may be worth it, but just like any other drug, there is a cost-benefit ratio.

■ HOW WILL THE RECENT LEGALIZATION OF RECREATIONAL CANNABIS CHANGE THE MEDICINAL CANNABIS LANDSCAPE? DOES THIS HAVE ANY IMPLICATIONS ON YOUR LINE OF WORK?

In terms of the existing medicinal cannabis framework in Canada, we don't really know what the recent legalization is going to do. One possibility is that medicinal cannabis and recreational cannabis will exist side-by-side and there won't be much difference. The other possibility is that a lot of the licensed manufacturers that produce medicinal cannabis move over to the much larger recreational market and may produce fewer products in demand from this minority medicinal market —things like high-CBD products. Thus, there may be a change in the availability of the product based on the change in legislation. There are so many questions surrounding the legalization because we don't know whether the overall prevalence of recreational and medicinal cannabis users will change and whether there will be changes within subpopulations. One interesting thing is that we haven't seen a reduction in the rate of individuals seeking medicinal cannabis leading up to legalization. It seems like if people simply wanted access [to cannabis], they would just wait for legalization to happen. The fact that people are still seeking authorizations and meeting with physicians suggests that there is still going to be a robust segment of the population that wants to use medicinal cannabis. Another conjecture is that maybe the medical users will simply say, "I don't need to pay more [for medicinal cannabis] or pay for physician visits," because those are out-of-pocket and typically unreimbursed expenses, and instead buy recreational cannabis. If we had suddenly seen a plateau or a decrease in the number of people seeking authorizations, those would be people who see the official announcement of legalization as a signal that they'll be able to get [cannabis] without an authorization. I tend to think that there will still be a distinct [medicinal] market but we don't really know. This is why we're doing lots of research to study how attitudes and behaviours change over the course of legalization.

■ ARE THERE ANY INSIGHTS FROM THE OPIOID CRISIS THAT CAN BE APPLIED TO MEDICINAL CANNABIS?

The opioid epidemic is, in some ways, a not-so-obvious but still very relevant reason why we created the CMCR. One of [the] things that the opioid crisis has revealed is how dangerous opioids are in terms of their abuse liability. Unforeseen consequences can happen when potent psychoactive drugs enter widespread medical practice with an underappreciation for their risks in the industry, among physicians and patients. It's not too long a line to draw to expect a similar set of challenges when it comes to medicinal cannabis. You have a skyrocketing trajectory of use. We have a culture and industry that are fairly favourable toward the medical benefits. I would say that we often have an underappreciation of associated risks. Now, along with the legalization of cannabis for non-medicinal purposes, we have a major change that will provide even greater access to the general population. What we very much hope is that we don't have to learn the lessons from the opioid epidemic twice. There are good reasons to think that that won't happen. One of the things that makes the risk profile of cannabis lower than that of other drugs is that it has virtually no toxicity in terms of life-threatening levels of consumption. You can certainly overdose on cannabis. You can consume too much and have very unpleasant symptoms, such as delirium and psychosis, which should not be trivialized. But, unlike opioids, the risk of overdose leading to death is virtually nil. So, that kind of lethality dimension is not present. However, that doesn't mean that there won't be other unforeseen consequences. Part of our focus is trying to be a vocal proponent for knowing the risks of cannabis and investigating the potential benefits. I want to emphasize that we're neither pro-cannabis nor anti-cannabis. We're pro-research and we're really trying to promote an evidence-based understanding of cannabis.

■ WHAT IS THE DAY-TO-DAY EXPERIENCE LIKE AS A PRINCIPAL INVESTIGATOR?

The day-to-day experience is probably not the most glamorous, I would say. It involves mostly either being in meetings, writing and analyzing data, or writing results, which probably doesn't seem very interesting. But, the great part about the work that we do is the fact that we are very trans-disciplinary in the CMCR. I'm a clinical psychologist, but probably half the affiliated faculty are physicians, many of whom are clinician-scientists, meaning those who are both seeing patients and doing research. And then we have a lot of PhD scientists who are doing more basic research. A lot of the meetings and studies we're designing involve talking to people who are doing very different things and have different ways of thinking about the world. It means that we can ask some fascinating questions.