Aaron van Dorn (00:07):

Welcome to AJP Audio for October 2022. I'm Aaron van Dorn. Today on the podcast I spoke with Dr. Richard Davidson from the Center for Healthy Minds at the University of Wisconsin-Madison. Dr. Davidson and colleagues investigated the effects of mindfulness training on the neural mechanisms of pain. After that, I once again speak with American Journal of Psychiatry Editor-in-Chief, Dr. Ned Kalin, about what else is in the October issue of AJP.

Aaron van Dorn (00:27):

Dr. Davidson, mindfulness training has long been used as a component of pain management. Your study was investigating the effects of mindfulness training on the neural mechanisms of pain. What did you find?

Dr. Richard Davidson (00:37):

Well, first, before I get to the details of the study, let me just say that the search for nonpharmacological, and we might say complimentary strategies, to cope better with pain, to modulate pain, is something that is increasingly important in our society today. Particularly given the crisis that we're facing with opiate addiction.

Dr. Richard Davidson (01:08):

This study, I think, is broadly relevant to those concerns. This study was part of a large-scale effort that involved multiple components, one of which was to investigate the impact of short-term mindfulness meditation training on pain. And then a second component was to investigate how people who've been doing mindfulness and other meditation practices for a much longer duration of time, we might consider these to be experienced meditators, how they differently process pain compared with age and gender-matched controls. We investigated the neural basis of pain processing by examining changes in the functional MRI in response to a painful stimulus. And so we delivered pain with a heat stimulus in the scanner, and here is in essence what we found.

Dr. Richard Davidson (02:18):

We first found that short-term mindfulness training indeed changes a neural response to pain that had been delineated in prior research. And what do I mean by this? What I mean is that there has been a body of scientific literature on how the brain responds to painful stimuli. We know exactly where to look, so to speak. And using this predefined measure that is called the neural pain signature, we found that over the course of two months of learning mindfulness meditation, the group doing mindfulness training showed a significant decrease in this neural response, compared to a very carefully matched control group that was matched on all of the, what we would call, nonspecific characteristics. That is the expectations that people have, the group support, the weekly meetings, all of those were very carefully matched. And we still found that the mindfulness group showed these specific neural differences compared to this other group.

Dr. Richard Davidson (03:40):

When we examined long-term meditators we found something quite interesting, and that is that they also showed some differences in the neural processing of pain, but they were different than the short-term meditators. Where we saw the long-term meditators showing effects was in a different kind of neural signature, it's been called a stimulus-independent signature. And what do we mean by stimulus-independent? These are the brain regions that are involved in both the emotional response to pain, as

well as efforts to modulate pain. And they're not directly linked to the intensity of the nociceptive or painful stimulus that is used.

Dr. Richard Davidson (04:34):

And with the long-term meditators, what we find is something that we did not predict, which is that the more cumulative practice they had based on a structured interview that we do with them to assess their lifetime practice, but specifically during intensive meditation retreats, the more practice they had during these periods, the greater the reduction in this stimulus-independent neural signature for pain.

Dr. Richard Davidson (05:08):

Those are the key findings that emerged from this study. And to broadly summarize at a much higher level, what we know from this study is that meditation does change the brain's response to pain. The changes that you see in beginning meditators are different than the changes that you see in long-term meditators, and that practice matters.

Aaron van Dorn (05:34):

While we all experience pain, it can be extremely difficult to describe or quantify. How do you go about investigating pain?

Dr. Richard Davidson (05:41):

Yeah, it's a great question. And so the way we go about investigating pain is in this case through two primary modalities. One is by asking a person to report on their pain and different dimensions of pain. You can ask them to rate the extent to which the pain is unpleasant. You can ask them to rate the intensity of their pain, which they're typically correlated, but not necessarily perfectly correlated. And then you can also assess how their brain responds to pain.

Dr. Richard Davidson (06:18):

And so by looking at the conjunction of the self-reports of pain and the changes in the brain in response to pain, we can make inferences about how meditation changes our response to pain.

Aaron van Dorn (06:36):

You mentioned the group that you investigated of long-term meditators earlier, but while they reported less subjective pain than other groups, you didn't see that in the neural response that you took. What does that suggest?

Dr. Richard Davidson (06:45):

It suggests a few things. One is just to be sure to include the other finding that we reported, although there was not an overall difference between the long-term meditators and the age and gender-matched controls in their neural response to pain. There was a very strong association that we reported between their length of practice during retreats and their neural response to pain, with more practice associated with a decreased neural response to pain. And this is specifically the stimulus-independent variety of the neural response.

Dr. Richard Davidson (07:26):

And what it suggests is that although the long-term meditators are reporting overall less pain than the non-meditators, the standard neural responses that we measure are not showing that. And it suggests that the difference is not in the sensory representation of the pain, but it is probably more what we would say downstream in how the pain is interpreted. Another way to put this in more colloquial language, is that it's not so much that meditation is changing the pain itself, but it may be changing our relationship to the pain so that we can more effectively cope with the pain.

Aaron van Dorn (08:22):

Pain management is an issue of great concern, especially given the obvious problems that we've seen with the use of opioids to manage pain. What do your findings suggest about pain management practices, and are there any clinical implications for your findings now?

Dr. Richard Davidson (08:33):

I believe there are important clinical implications right now. The clinical implications are that the strategies, the simple mindfulness strategies, particularly from the naive meditating group that we studied who were taught mindfulness practice over the course of two months, that this strategy is one worth examining as a compliment to other approaches for pain management.

Dr. Richard Davidson (09:05):

And the conjecture from these data is that using this mindfulness technique as a compliment may not eliminate the necessity of also using a pharmacological approach. But it may decrease the dosage, for example, so that we don't have to use as much opiates in pain management. And it may enable people to withdraw from opiates more quickly when they have this complimentary strategy that they can do anywhere, anytime.

Aaron van Dorn (09:45):

Were there any limitations for your study?

Dr. Richard Davidson (09:46):

There are always limitations in any scientific study. And so yes, there were some limitations. It would be ideally great if we were able to study the longer term effects of this.

Dr. Richard Davidson (10:02):

And so one of the important questions is whether the change that we saw after two months of meditation practice is preserved for a long period of time, and we don't know the answer to that. We also don't know how this applies to chronic pain. This was a study where we were inducing acute pain in the laboratory. And so the extent to which this generalizes to chronic pain conditions is something that requires further study.

Aaron van Dorn (10:40):

Speaking of further study, what's next for your research?

Dr. Richard Davidson (10:42):

One of the things that we are excited about is the opportunity to disseminate these kinds of strategies more widely. We have an affiliated non-profit organization associated with our university research

center, and we've developed an app that is freely available, called the Healthy Minds Program. And because it's freely available and can be used exclusively remotely, it's a way to disseminate this kind of training more widely.

Dr. Richard Davidson (11:15):

And we are interested to see whether this approach of doing this digitally and fully remotely is effective in modulating pain. And if it is, it's possible to scale this much more easily and much more widely. So this is one important question on the docket for the future.

Aaron van Dorn (11:40):

Dr. Davidson, thank you for taking the time to speak with us today.

Dr. Richard Davidson (11:43):

You're most welcome. Thank you for the good questions.

Aaron van Dorn (11:46):

Up next, Dr. Ned Kalin. Dr. Kalin, welcome back to AJP Audio.

Dr. Richard Davidson (11:50):

Thank you. It's great to be back.

Aaron van Dorn (11:51):

This month, AJP has some interesting articles looking at opioid use disorder, cannabis use disorder, and an interesting look at mindfulness training as it relates to pain treatment, which I discussed earlier with Dr. Davidson. Let's start with that article.

Dr. Ned Kalin (12:01):

Sure. This is, I think, a potentially exciting paper, and it really nicely fits in with the other papers in this issue that are related to opioid use disorder and cannabis use. This is a study that was done at the University of Wisconsin by Dr. Davidson's group, that examined the efficacy of an eight-week mindfulness-based stress reduction training intervention on individuals' capacities to regulate their pain responses, both in their brain and as they feel pain in their bodies.

Dr. Ned Kalin (12:31):

In this particular study there were three groups. There was a group that received the mindfulness training. There was a group that was what we consider an active comparator group, where individuals participated in a health enhancement program but did not receive mindfulness training. And then there were also a group of individuals that remained on the wait list.

Dr. Ned Kalin (12:51):

And the way that this work is that these were not patients, these were healthy individuals. They were placed in a scanner. And while in the scanner, experienced varying intensities of thermal heat-related pain. The long and the short of this is that the investigators found that both active interventions reduced the subjective feeling about pain, that is to say that the participants rated pain as being lower after the interventions. But in the group that received the mindfulness-based training, there were changes in

brain function that were identified in neural circuits and patterns of neural circuits that have to do with their responsivity to pain, as well as the more psychological, cognitive, emotional processing aspects of the painful experience.

Dr. Ned Kalin (13:38):

And so this is, I think, a really interesting early paper on thinking about using nonpharmacological means to manage pain, and especially as an alternative when we think about other types of painful conditions that require opiates, where we're concerned about overuse of opiates or opiate misuse.

Dr. Ned Kalin (13:58):

A couple of issues to point out here, one is that this was done in a normative population. It wasn't a patient that had psychiatric problems and it also wasn't a patient that had pain problems. And the extent to which this works and a chronic pain population or sample remains to be determined. Nonetheless, it's really an interesting beginning way of thinking about how we can help our patients better manage their pain without medications.

Aaron van Dorn (14:21):

Next up we have the first of two papers about Dr. Hasin and colleagues. This one on opioid use disorder.

Dr. Ned Kalin (14:25):

Yeah. This is a paper that is interesting from the standpoint of the fact that it addresses opiate use disorder in pain patients that are being treated with opiates. And we actually have another paper that's related to this as well, which we'll talk about.

Dr. Ned Kalin (14:41):

But in this particular paper by Hasin and colleagues, the investigators look at different ways of thinking about diagnosing opiate use disorder in pain patients that are treated with opiates. And this gets to be somewhat of an issue because the medications are prescribed for bonafide painful conditions. And in addition to that, anybody that's on these medications for a period of time will develop tolerance and dependence types of symptoms. And when stopped, will have withdrawal symptoms. And tolerance and withdrawal are typically criteria for DSM-5 from the standpoint of opiate use disorder. Although when diagnosing opiate use disorder that is related to the prescription of opiates, those criteria actually have been dropped.

Dr. Ned Kalin (15:27):

And again, to get to the results, what the investigators found was that when they adjusted their criteria by either leaving out the pain criteria or leaving out the tolerance and withdrawal criteria, not surprisingly, the numbers of individuals that had this diagnosis decreased. And in the end, the investigators felt that by dropping the tolerance and withdrawal criteria and also the pain criteria, that the diagnosis was probably a more valid diagnosis for opiate use disorder. This was done using an instrument called the PRISM-5, which is an instrument that gets at opiate use and maybe a good useful tool at some point for clinicians.

Dr. Ned Kalin (16:11):

And then finally, we have an editorial that accompanies this by doctors Mark Sullivan and Jane Ballantyne from the University of Washington, and they comment on the paper. But the point that they make is that regardless of where you draw the line diagnostically, in individuals that are prescribed opiate medications for pain, if they're on them long enough and at high enough doses they will develop the characteristics that are associated with opiate misuse, which include dependence, tolerance and withdrawal, which we need to be very wary about in treating our patients.

Aaron van Dorn (16:40):

Following that, we have a paper from Jutras-Aswad and colleagues, looking at the treatment models for opioid use disorder. What can you tell us about that?

Dr. Ned Kalin (16:46):

This is also examining ways to treat prescription-related opiate use disorder, just as we talked about thinking about how you draw the line and make the diagnosis for that problem. And in this particular paper, the authors examine whether buprenorphine combined with naloxone, primarily taken at home, is an effective and safe strategy for the treatment of prescription-related opioid use disorder.

Dr. Ned Kalin (17:12):

This is what we call a non-inferiority study because what was compared was the sublingual buprenorphine naloxone taken at home, as compared to methadone, which was administered in a clinic setting. And I should point out that this was done in Canada, so has perhaps some specificity to Canadian delivery of care and medicine. And it also basically looked at outcomes from the standpoint of how stable individuals were with staying off their opiates, looking at urine screens to look at the percent of individuals that are opioid free, and so on.

Dr. Ned Kalin (17:47):

And so what the investigators found was that when they obtained the opiate free urine drug screens every two weeks, that was the primary outcome measure. 24% of the screens were opioid free in the buprenorphine naloxone group, compared to 18.5% in the methadone group over this period of study, which was 24 weeks. I should point out that the retention rates in this study were low, so that's something to keep in mind. And also, while there was a reduction in the urine screens, the reports on the quality of life did not differ between the groups either. And this is positive reports in the quality of life.

Dr. Ned Kalin (18:28):

Basically this clinical trial suggests the potential utility and safety of buprenorphine and naloxone in home-based treatments for individuals suffering with prescription-related opiate use disorder. And it's particularly relevant during times where it's harder to get to the clinic, especially during COVID times, which we have just seen. And also this is an opportunity for individuals that don't have the resources or that there are barriers to get to the clinic, so individuals that are under resourced could theoretically be treated at home this way.

Aaron van Dorn (19:02):

Another look at opioid use disorder, this time from Dr. Lin and colleagues, looks at the impact of treatment during the era of COVID-19.

Dr. Ned Kalin (19:08):

This is a related theme. As the paper that we just talked about, it's trying to think about how we can do better from the standpoint of getting the numbers of people that are suffering from opiate use disorder treated.

Dr. Ned Kalin (19:21):

This is a study done in the VA population. And during the COVID period the VA actually relaxed some of the criteria, from the standpoint of getting into their opiate use disorder treatment program. And one of the changes that occured was that the initial evaluation that had to be in-person for buprenorphine treatment was basically dropped and this could be done through telehealth. And by so doing the number of patients treated with buprenorphine for opiate use disorder increased by about 14% over the period of the study, which was between March 2020 and February 2021. Not surprisingly, the number of telehealth visits went way up for this sample because that was actually the way they were being treated.

Dr. Ned Kalin (20:05):

But I think the bottom line is that more individuals were reached by this modification, suggesting that if the VA and other institutions were to move forward with this type of policy and other ways to think about breaking down barriers to treatment access, that this too would facilitate more individuals getting hopefully effective treatment for opiate use disorder.

Aaron van Dorn (20:30):

Finally, we have another paper from Dr. Hasin and colleagues, so this time looking at the impact of cannabis use disorder in US veterans. What can you tell us about that?

Dr. Ned Kalin (20:36):

Yeah, so this is looking again at a survey of the veteran population from their database from 2005 to 2019, and trying to track the changes and the rate of changes in the prevalence of cannabis use disorder. And the investigators were particularly interested in a variety of factors that would be related to increased or decreased use, including age, sex, race, and ethnicity.

Dr. Ned Kalin (21:04):

Not surprisingly, over time there has been an increase in the diagnosis of cannabis use disorder in the VA population, as we think about the trends in general. If, for example, in 2005, cannabis use disorder was most common in patients that were less than 35-years-old, it was estimated to affect 1.7% of veterans. In 2019, cannabis use disorder was estimated increased to affecting 4.84% of veterans in this age group.

Dr. Ned Kalin (21:36):

A couple of other details that are really interesting. In the 65 year and older age group, the diagnosis of cannabis used disorder dramatically increased from 0.03% to 0.4%. And again, the percentages are low, but that's about a tenfold increase. And this was in 2019. And also, in individuals less than 35 years of age, the rate of increase for cannabis use disorder was greater in Black individuals, compared to white individuals.

Dr. Ned Kalin (22:05):

So these are interesting data. They suggest that overall, and not surprising, there are increases in cannabis use disorder being diagnosed in the VA population. But in particular, one of them highlighted in this paper are the increased incidents in the older group, the 65 and year older group, and the increased rate of cannabis misuse in Black individuals that are 35 years or less, compared to other veterans.

Dr. Ned Kalin (22:34):

Again, we're excited about this issue because it really does highlight opiate use disorder and pain management, as well as cannabis use disorder. It's important to keep in mind that many cases of opiate use disorder are unintended, from the unintended consequences of prescription drugs for pain management. And we have two papers related to that. And also, drugs like opiates and other substances, including cannabis, are frequently used without a physician, but in a self-medication type of way, if you will, for anxiety, depression, and pain.

Dr. Ned Kalin (23:08):

Then some of the major takeaways in this issue are acknowledging the high prevalence of opiate use disorder, and in a review of paper that we feature to start with are reviewing the current evidence for its management. Two, thinking about how you make the diagnosis of prescription-related opiate use disorder and looking at different cutoff criteria for that, which includes dependence and tolerance, as well as withdrawal symptoms and treating the pain. Three, demonstrating that home treatment with buprenorphine and naloxone can be effective and is an easier treatment from the standpoint of an access issue. Also, other ways of reducing barriers to treatment for this population include modifications that the VA made in relation to not requiring an in-person visit for buprenorphine management and opiate use disorder, which increased access.

Dr. Ned Kalin (24:06):

And then finally, the really interesting paper on using mindfulness-based stress reduction training to teach individuals how to modulate their subjective sense of a painful stimulus, as well as demonstrating the capacity to activate the underlying neural systems that are involved in pain processing, and to modify those responses with mindfulness-based stress reduction training.

Dr. Ned Kalin (24:31):

So together the papers really do highlight the importance of developing new strategies that are aimed at reducing the incidence of opiate use disorder, as well as for treatment. Important to obviously decrease the use of prescribed and illicit opiates. Again, one way to get around this is to start thinking of non-opiate strategies, including behavioral strategies, one of which we present in the journal. And then finally thinking about really decreasing major systemic barriers to treatment, especially for minoritized individuals, marginalized individuals, individuals of color, that may have more difficulty accessing treatment. And really understanding that this is a critical public health policy issue that needs to be dealt with at a systemic level.

Aaron van Dorn (25:15):

Well, Dr. Kalin, thank you once again for speaking with us.

Dr. Ned Kalin (25:17):

It's my pleasure.

Aaron van Dorn (25:18):

That's all for this month's AJP Audio, but APA has other podcasts you can listen to. Check out Mentally Healthy Nation, Psychiatric Services from Pages to Practice, and the rest at psychiatryonline.org/podcasts.

Aaron van Dorn (25:29):

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