"Finding the Hurt in Pain" with Irene Tracey

Transcript of Cerebrum Podcast

Guest: Irene Tracey, Ph.D., holds the Nuffield Chair of Anaesthetic Science and is head of the Nuffield Department of Clinical Neurosciences at the University of Oxford. Tracey did her undergraduate and graduate studies at the University of Oxford and then held a postdoctoral fellowship at Harvard Medical School. She helped to co-found and for ten years was director of the Oxford Centre for Functional Magnetic Resonance Imaging of the Brain (FMRIB) at the university. She was an elected councillor to the International Association for the Study of Pain and chair of their Scientific Program Committee, is a Council member of the Medical Research Council, and on the Brain Prize selection committee. In 2008, she was awarded the Patrick Wall Medal from the Royal College of Anaesthetists and in 2009 was made a Fellow of the Royal College of Anaesthetists. In 2015, she was elected a Fellow of the Academy of Medical Sciences and in 2017 awarded the Feldberg Prize. Tracey is married to Professor Myles Allen, a climate physicist, and they have three children.

Host: Bill Glovin serves as editor of *Cerebrum* and the *Cerebrum Anthology: Emerging Issues in Brain Science*. He is also executive editor of the Dana Press and *Brain in the News*. Prior to joining the Dana Foundation, Mr. Glovin was senior editor of *Rutgers Magazine* and editor of *Rutgers Focus*. He has served as managing editor of *New Jersey Success*, editor of *New Jersey Business* magazine, and as a staff writer at *The Record* newspaper in Hackensack, NJ. Mr. Glovin has won 20 writing awards from the Society of Professional Journalists of New Jersey and the Council for Advancement and Support of Education. He has a B.A. in Journalism from George Washington University.

Bill Glovin: Today's guest on our monthly *Cerebrum* podcast is Irene Tracey, all the way from the oldest English-speaking university in the world; Oxford. Dr. Tracey is author of our article "Finding the Hurt in Pain." The article examines how brain imaging is opening our eyes to the richness and complexity of the pain experience. This includes such things as neurochemistry, network activity, wiring, and structures.

Dr. Tracey holds the Nuffield Chair of Anesthetic Science and is the head of Department of Clinical Neurosciences at the University of Oxford. She helped to co-found and for 10 years was director of the Oxford Centre for FMRI at the university. In 2015, she was elected a fellow of the Academy of Medical Sciences, and in 2017, awarded the Feldberg Prize. Welcome, Dr. Tracey.

Let's start with the article's interesting turn of the phrase title. Can you tell us what you mean by, "finding the hurt in pain?"

Irene Tracey: Sure, Bill. It's a pleasure to be here with you all. I was interested to write this article to communicate to both the scientist and the interested lay-listener or reader. The challenge we have as either pain scientists or pain clinicians and for

pain patients ... Anybody out there that has pain. As to what it is we've been discovering to unravel this mystery of why it is that pain hurts, what's the point of pain hurting, and importantly, when it goes wrong in chronic pain sufferers, where is that hurt based and whether the science can help us try and come up with better ways of treating both acute and chronic pain.

For me, I wanted to describe some of the excitement in science. I wanted to alert people to the fact that pain's been around for a long time; it's one of our oldest sensory and emotional experiences. And yet we still haven't really nailed this question, and ... Well, we've got the question, but we haven't nailed the answer to the question, in terms of, what actually constitutes the hurt experience in pain?

Bill Glovin: Hmm. I couldn't help but notice that your husband is a climate physicist at the university. I'm sure you consult with him on raising your three children, but do you ever consult with each other on your respective disciplines?

Irene Tracey: Absolutely. I think for a lot of people who are in sciences, even though you work in very different topics and areas, there's a commonality about science, both in terms of the approach one uses and the philosophy and the logic behind how you formulate a hypothesis, and how you go about testing that question and that hypothesis with experiments or with theory, and then interpreting the data accordingly.

Then, when you're working in the physical sciences, as he is in climate physics, and in my own technique of neuroimaging, which requires quite a lot of computation and mathematical algorithms and methods to analyze the data that we're getting from the human brain, actually, there's surprisingly quite a lot of commonalities in the methods and the image analysis and the data analysis approaches that we both use.

We find, often ... It's not quite pillow talk, but certainly over breakfast or dinner, we do talk about, sometimes, the experiments and where, maybe, we're struggling a little bit with a different way of maybe trying to analyze the data.

Then he'll share what they're doing in the physics world, and there's been some quite nice examples of where both sides have benefited each other. In one instance, some of our image analysis software ... One of our image analysis guys has used some of what we call the Brain Registration Methods, where we're able to register everybody's brains into the same sort of space and move people's brains around if he likes them. We can be sure that a blob of activity in one person's brain can be represented similarly in another person's brain, and that approach can be applied to weather patterns, and the movement of clouds from one day to another, and trying to rearrange and overlay things, and register, again, complex weather patterns in a similar way.

Then, vice-versa. Some of the work that my husband's been doing, looking at how you would predict a next event, if you like, we can apply to some of our brain imaging data, more related to our work in anesthesia and how the brain goes to sleep during anesthetics. Again, we've taken some of his algorithms and applied it to our own data, so that's been really exciting.

Bill Glovin: Hm. Is there anything in your life experience that inspired you to devote your research efforts to better understanding pain?

Irene Tracey: Not particularly. I mean, I was a very sporty individual growing, so I was always in various teams. I was a hockey player. And a rower and things. I did have a bad knee injury playing field hockey during my doctorate. I really busted my knee badly on AstroTurf, so I had to have an operation, and of course, willingly volunteered myself to be on the post-operative trial for analgesics. I was put, sadly, on the sham one, so I was not given any, and then really witnessed myself really painful post-operative pain, which went on for hours and hours. They actually then forgot that I was on the trial and forgot to give me some meds about four hours later, so I was really suffering for quite a long time. I'm not going to pretend that was what alerted me, but certainly, it made an impression on me that, wow, this is quite an extraordinary experience.

As I was moving into neurosciences at that point, using again brain imaging, it struck me that this was an area that we really knew very little about, and here were some tools, these non-invasive brain imaging tools, where we could actually look at the very organ, the brain, from which the perception of pain arises. It struck me then, actually, even your experience of pain can change quite a lot due to things like whether you're attending to it or distracting and depending on your mood. I was, again, reflecting on that experience for myself, interested to know whether those influences ... How do they play out at a physiological level because of what brain networks are bringing; are coming and being used to make that pain experience worse if you pay too much attention to it or if you're very anxious about it?

That was an experience that happened to me, and it was going to the States and doing a post-doc there for couple of years, which really consolidated the fact that I wanted to move the magnetic resonance techniques that I was trained in into the area of neuroscience and then specifically into the area of pain. It was that journey, I guess, that brought me to where I am today.

Quite often, in science, there isn't a lightening-bolt moment, but subtle things happen on your life journey that intrigue you or are just there, latent. On that journey of life, you realize, actually, they've been influencing you and guiding you on the path to why it is you end up, as an academic, working specifically in a particular area.

Bill Glovin: Do your kids or other people tease you about pain as your discipline?

Irene Tracey: Oh, yeah. No, I get a lot of teasing about that. People are pretty terrified of pain, and rightly so. It's something that everybody has experienced in their life, and so I think it does puzzle people, and it intrigues people why you would choose to work on it. But then, in conversation, quite quickly they realize, "Yeah, actually, wow. This is something that's actually so old, both in evolution terms, and so important in terms of its warning, and so intriguing." That's why philosophers have puzzled over it.

The fact that it's such a subjective, private experience. It's something that's just really hard to know and understand, and it has all these societal influences of biases in culture. It's, of course, got this great clinical need, but suddenly, when you unpack it, you realize there's an awful lot to it. I think, then, people quite quickly realize, "Yeah, actually, that makes total sense, why you'd want to, as a neuroscientist, particularly using these non-invasive techniques, direct all your energy and attention to that," because it allows you to really answer some very fundamental questions about the brain and how it works, and perceptions and what we mean by perception, but also understand a very fundamental experience that we all share.

But then it's also got this huge clinical relevance. Again, I think a lot of society is really unaware of just the enormity of the chronic pain problem in modern society.

Bill Glovin: Boy, if you were my mom, you'd be wide open to some quips about the fact that my mother's an expert in pain because she delivers it to me all the time. We won't go there.

Irene Tracey: Exactly. Yeah, no, I could threaten my kids, because we've got all sorts of weird and wonderful ways we can inflect pain on our subjects. All ethically allowed, I should quickly add, but sometimes ... I'm also a Roman-Catholic, so of course, one gets teased a little bit there that that sort of goes with that territory, too. This is really the reason that I work on pain.

Bill Glovin: Oh, boy.

Irene Tracey: No, but for my kids, yeah, sometimes I can whip out, "All right, guys. I'll take you to the lab if you don't eat your dinner or you don't go to bed." It can be quite handy.

Bill Glovin: Yeah, that's great. Why is it that two people who experience the same injury experience pain differently?

Irene Tracey: Oh, that's a great question, Bill. Well, we're still trying to understand that. I think, historically, we thought that was largely explained by their attitudes and maybe their cultural upbringing as to what level of expression they were taught to give to something averse and unpleasant like pain. I think we're quite confident now in the last decade or so with, again, research, and both from a

genetic level and at a what we call systems neuroscience. Again, looking at the whole person with, say, technically you can see what's going on inside the brain and the spinal cord.

But we're more clear now that these differences aren't and cannot simply just be simply explained only by cultural differences. They really are physiological differences that are genetic. Variances in people's genes will influence their threshold. Variances in how they have been brought up; the whole sort of nature-nurture influence. This conflict of the epigenetic profile. The idea of how your genes are altered, if you like, dependent on your environmental influences as you develop.

I think people should remember that the central nervous system is very rapidly developing from a baby through to infant years and adolescence through to adulthood. Your life journey and all the bumps and scrapes that you've had on that journey, and the different experiences you have both psychologically and physically and culturally, will all influence how your central nervous system has been wired up. Increasingly, we think this is really quite important, now, for what it explains.

Not only just the differences in, if I gave somebody a phony burn, how they would describe that as maybe more intense or less intense, but importantly or more importantly, it might explain why one individual ends up, to what seems like the same injury, in a persistent, chronic pain state, and somebody else recovers from that after three or four months.

This idea of a resilience or a vulnerability in your central nervous system towards developing particularly persistent, chronic pain, and I think for a lot of other central nervous disorders and diseases as well. I think the neuroscience community is getting more confident. It's still early days, but we're getting more confident that these influences really probably can explain a lot about why one patient ends up on one trajectory and another ends up on a different one. It comes down to these issues of vulnerable networks and resilient networks, and that's a big part of what we're trying to understand and research. What are those networks? Can we fix them? Can we un-wire bad wiring, if you like, and make it better again? What can we do to make a vulnerable central nervous system a resilient one?

Bill Glovin: Since I think you're alluding to the fact there is a genetic and perhaps cultural tie, have you found that there are some cultures where the people are more resilient or can withstand a greater amount of pain?

Irene Tracey: We don't do research on that, but certainly, the pain community is very interested in these questions, and there are some large studies being done in various countries. Studies being done with twins who have, again, a shared genetic background but different upbringing experiences. Some communities which have been quite remote and so quite homogenous in their gene pool.

That data's being gathered at the moment, and the genetics being looked at. There's no particular answers yet, but we hope that that work that's ongoing and, again, quite recent, will give us some clues as to what are those explanatory factors as to why some people are more resilient and more stoical and others are not.

Certainly, we know just by observation and anecdotally, that certain, in going to the cultural influence, that certain cultures are a different... I don't mean to be glib, but more Nordic countries where, again, the expectation is not to express, necessarily, so much the suffering. Again, there are studies being done looking at, again, how women tolerate through childhood compared to other countries where it is encouraged to be very expressive and very, if you like, Latin and very vocal and passionate about describing your pain.

Again, this is an expression. The way somebody describes and reports their pain is another component to the whole picture of pain, if you like. What we need to understand is what is going on physiologically in the background, in terms of what their experience is, which might be very, very, related to how they express it, or it might be different to how they express it, because they're expressing it due to a cultural influence, but actually, what they're feeling physiologically, if you like, might be quite similar between two different cultures, but the way they describe and express it would give you maybe the impression that they're feeling it more or less.

All these things are very interesting. What we're looking at is the same, again, for men and women. The question I often get asked is, do men ... The sort of man flu thing. Do they really feel it more? That is an area that we're doing some work on, and looking at, again, differences in how hormones and differences in hormones play out.

Even the difference in hormones that women experience throughout their period and their monthly cycle, how does that influence their experience? These things, I think, have quite surprised us, how powerful they are at changing the way these signals are processed and changing the experience.

Early days, but again, it's an area of science that people are now more going into. It's very important because this touches on what we call social neuroscience, where you're asking questions about society and cultures. These things, which I think, historically, haven't been studied as much under the broad neuroscience umbrella, but they're really, really, important for us to understand.

Bill Glovin: Fascinating. In your article, you write a lot about the placebo effect. Can you tell us about what the placebo effect means in pain research?

Irene Tracey: Yeah, it's very important. I mean, the whole concept of placebos has always been closely linked to pain and pain relief, and this goes back ... Well, it goes

back to when time began, where people didn't have drugs, and lotions and potions were given to individuals and without any proof of efficacy, and people would have good efficacy from them. That was understood, they really believed there was some active agent in there, but chances are there was nothing and it was very much a placebo effect.

Formally, really recognizing the idea that you could have placebo analgesia was really understood better during the first and second world wars. Henry Beecham was a really pivotal physician, who really proved significantly in the statistics that the placebo effect ... Giving soldiers saline injections rather than morphine had similar good pain relief effects. Therefore, this placebo analgesia, in an absence of an actual agent, was a true thing and existed and was very, very, powerful.

What's interesting about it, and what I tried to touch on in the article, is, actually, the almost irony of how we use the word placebo and what it means. I think what the science has taught us, particularly neuroimaging in the past decade and a range of different experiments, is what the physical basis of placebo analgesia is. How is it and why is it that people have analgesia? What is the network that's being used?

We're very clear now on what that is. It's probably an area that, in terms of different brain science, that we know best, as in the pain sciences, is about the placebo network. What's interesting is it's the network that we use when we distract ourselves from pain. They're very old networks centered in the brain stem. We use it a lot when we're maybe watching a very gripping movie, or are very distracted on the sports field and we don't feel the pain of the injury. Then afterwards, when that hierarchal situation is over, you suddenly realize, "Oh my goodness. I've been cut and it's really sore," and you feel that pain, but you've blocked it at the time.

This is a very powerful network, and that's the network that placebo analgesia hijacks, and uses. There's nothing particularly special about it, but it's using a very old, very powerful endogenous system that the body has given us in order to combat pain in situations where we don't want to be distracted by the pain because we have something more pressing to deal with.

Quite a few of us are really quite keen to reframe placebo, because the word placebo comes from the Latin. The word that placebo chants in Latin was used by monks who were hired and paid money to in order to come and mourn at your funeral if you didn't have any friends. The very word and what it means and what it signifies is fake and fakery. You have this whole problem around the use of the word and people's impression of what the word means; that they equate, if you had a placebo effect, well, then you didn't really have the thing in the first place, so you were faking it.

That couldn't be more wrong. It's a flawed understanding of what a placebo's active manipulation is. I think the science in the past decade has been really important at raising, in society and in ethics committees and in drug trials and, "What do we mean by the placebo arm?" ...

Actually, what do we mean by the placebo arm, and is that the right word that we should be using? Do we really all now understand what we mean by that? And how does that change the way we fundamentally think about a whole host of situations where society thinks they know what is meant by placebo, but actually, the science is telling us we should rethink it?

Bill: Speaking of faking then, how does this differ from, let's say, a psychosomatic disorder?

Irene Tracey: Well, that's, again ... People have different definitions of what they mean by that. Maybe if I re-describe ... Possibly, what you're asking is this very challenging question of people having pain where you can't determine what the origin of the injury is.

We're very comfortable when we can see some physical damage, often in the what we call peripheral part of the body, or somewhere that we could see its structurally damaged internal organs, or a gash on the skin, or a crushed knee, or something. We're very comfortable when we see damage equals pain. What we're not comfortable with is when we can't see with our crude technologies where the damage is, but the person says they're in excruciating pain, or we see what we think is not very much damage, but the persons says they're in excruciating pain. And we bring all sorts of judgements as to, well, it can't possibly be that painful for that level of damage. This is where biases of our cultural bringing come into play. Really, it can wreak havoc in understanding and appropriately diagnosing and treating and respecting an individual's pain, which will always be paramount to what they say it is in their subjective experience.

Psychogenic pain is the word that's been used for pain where you can't determine and show what the peripheral cause might be. And again, a bit like with placebo, is, unfortunately, people have a negative impression of it and then a negative usage of it, which is quite incorrect because psychogenic pain is genuine pain. It's not a second-class citizen to physical pain, where I'm being cautious now that I'm using a definition that's not mine but one that society likes to use, which is pain that you can see a damage area to.

Pain is pain, and pain emerges when the brain gets it. I don't disambiguate what the origin of that is, and I don't rank first order, second order, if I can see the physical peripheral origin of the pain or whether it is what we call centrally-generated; brain-generated. At the end of the day, the brain is the organ that produces the experience of pain, so if the appropriate regions are active and switched on for whatever reason, and that person is experiencing pain, then they are having pain.

That speaks to the very core definition that the International Association for the Study of Pain, which is the largest worldwide international authoritative organization interested in pain in its scientific sense and it's clinical sense. Our very definition of pain is a sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage. That very definition speaks to the fact that you don't actually have to have actual damage; you have the potential to have damage, and it's essentially an emotional experience described in those terms. Therefore, I think half of our definition allows for the fact that pain of whatever origin is real, and we should understand what the origin of it is because that will help guide how to treat it.

Bill Glovin: Let's shift gears for a minute. Last week, you were a featured speaker in a seminar entitled “Evidence of Pain from the Legal and Neuroscientific Perspective: Challenges and Pitfalls.” In your view, can or will we ever be able to use imaging to quantify the impact of pain in terms of jury awards from injuries?

Irene Tracey: That's a great question, and it's one which, again, as ... These conversations that many of us are having with lawyers and judges and personal injury lawyers, based on this side and your side of the pond, it's a very ... It's a question that has great topical relevance right now. People are very interested in this. I think, in the West, you have many companies that are offering this service.

I have to say, from the pain community, we're very skeptical of that use at this point in time. We're very nervous that people are using it when the technique is not ready yet in that way. Certainly, not at the individual level. But the science is just not there to back that up yet. We are, in fact ... A combination of people from different countries are producing a series of recommendations as to what one should be thinking about when wanting to use the technologies to prove or disprove or quantify the magnitude of pain in order to appropriately give the right award for, say, disability benefit.

What would need to be done to get the technology at that level? I think, at this point, it's fair to say that we're not sure it will ever get there, at the absolute DNA fingerprinting-type level of evidence. I think many of us are very confident that the tool's got incredible capacity to tell us a lot about the mechanisms that constitute people's pain; that tell us, and can be hopefully used, going forward, as a diagnostic tool. If we can get it to that level in the next decade or so, then there might be some use for it by certain cases, where it would be another component of almost diagnostic evidence, as just one piece of evidence amongst many other pieces of evidence, to help explain and understand why this particular individual is in pain. But to be used as a simple on-off binary lie detector, then no.

I don't believe it's appropriate to use it in that context, because I don't think that's really what you're doing with these brain imaging techniques. Pain is not this binary experience. What brain imaging can do is really help you understand and explain the person's pain, but to use it as a sort of intensity gauge where

you're quantifying how much ... This person's 4 out of 10 is equivalent to this other person's 7 out of 10. I think it's very dangerous to use in that context.

Bill Glovin: Are there any other neuro-ethic issues that are tied to pain and imaging?

Irene Tracey: Yes. Well, in terms of pain and imaging, I think the main one at the moment that we're struggling with is this one, because it is used already by companies for lawyers, and there's concern that that's galloping off at a pace that we're not comfortable with yet that there's validity. Hopefully, my description says where we're at and what we hope needs to be done in order to deliver on that one.

Of course, there are other ethical areas which pain impacts society, too. I think some of the challenging ones, which again, they're linked a little bit to why lawyers would want to use it in this context, is where there isn't the luxury of having the subjective report; the description by the individual. It might be because they are babies. Maybe they're premature babies in neonatal units, who you don't know what level of pain or suffering they're in. It could be in comatose patients in intensive care units. Patients who are having operations who are anesthetized. Our elderly who are maybe cognitively impaired and have dementia, and are unable to display or describe that they have some painful condition.

There are these other areas where I think we are challenged in understanding what pain are they in. First of all, are they in pain? If they are, what level of pain and should we, therefore, treat it, even though we don't know actually what's going on and they can never tell us?

This is where I would hope that, again, some of these tools could be helpful in giving us some of the, what I call, behind-the-scenes information as to what's going on; what might be underpinning what you think might be a behavioral display of discomfort and pain, but you don't know because they can't tell you. Again, this is all new areas for us to go into that, again, is relevant clinically, but also just relevant more broadly to society.

I think some of the other areas, where I think, again, as pain scientists, we have to be mindful of our ethical duties to society, is in situations where people want to use pain for torture. People want to avoid pain, maybe on death row. Again, where you are brought into and asked and, again, inappropriate demands on pain scientists, possibly. We have codes of conduct and guidelines under our societies in order not to abuse our knowledge and our understanding in those situations where pain is used as a weapon.

Bill Glovin: You talked about potential biases inherent in a clinical assessment. What are some of those biases?

Irene Tracey: Yeah. Not so much the clinical; it's more just as people, growing up in society, where there's a lot of subliminal messaging about toughness and pain and, "No

gain without pain, " and it's good to go through childbirth with no pain relief. There's a lot of messaging out there, and a lot of historical messaging in our literature and in our religions about the virtues of suffering in this world to gain in the next. Without realizing, we arrive as an adult with some, again, implicit, probably, biases towards what we expect people's pain to be, how much people should complain about their pain, et cetera, et cetera.

It's impossible to divorce yourself from those biases, but I think to recognize that you have them, and then when you are confronted with an unexplained pain and you think, "Well, hold on a minute. It can't be as much as that, because blah blah blah," to catch yourself out and remind yourself that, actually, "Hold on here. This is what the person is describing, and I need to be open-minded about this and balanced, and I mustn't bring some of those attitudes of what my pain experience is, and what I would do if I had pain like that, to the table." That's hard because that's naturally what we do.

I think, again, looking back to, why do we as living mammals display pain and report pain and grimace and give these very clear behavioral manifestations? It's in order to elicit a reaction in your fellow man, or your fellow animal, so that you are looked after and cared for. It's a very complex social contract, the pain. Again, that can be a very beneficial thing because it can provoke empathy and kindness and caring, but it can also provoke resistance and biases and neglect, if you like, and attitudes that, again, can mask and confuse. I think we just have to be careful about some of those things.

And again, I think, historically, going back to that placebo thing, it used to be the case that, in medicine, people did placebo tests on patients to catch them out, and if they got caught out and had a placebo analgesic effect, then that was the elimination test that they didn't really have a pain problem. It's one of many descriptions of where, again, that was the knowledge as good as it was then, but the new knowledge tells us that's based on flawed science. Luckily, that doesn't happen anymore.

Medicine science progresses as we learn and, again, pain's been a very good illustration of that as that sort of rule, if you like, that as the science tells us something, we rethink about how we conduct diagnostic tests and how we conduct interviews and conversations that are had between physicians and patients.

Bill Glovin: Your research, I think, has well-established that when people feel sad, their pain is worse, but is it possible to measure emotional swings with imaging?

Irene Tracey: Yes. In that experiment, we made people sad and then we made their mood neutral, and we gave them the same thermal burns throughout the experiment, and showed that they both felt ... They described that pain as more painful. Then we looked with the imaging, was the brain more active when they described it as more painful when they were sad? We showed that it was. That's

the same as burning them more, if you like. There was just a sadness amplifier inside the brain, and we worked out the circuitry by which it did that.

Part of that experiment, we did also just look at what was the brain activity during just the sadness condition itself versus the neutral mood condition. Again, I don't work in mood disorders. Many people use neuroimaging to look at moods. Again, both in the everyday setting and in the clinical setting. Certainly, that's a very rich area of neuroimaging, where really interesting insights have come about, about what is the fundamental basis of anxiety and depression and some of these very key components of emotions. What do we really mean by an emotion? Is that a physical thing can be labeled to brain regions, or is that something that is, again, a societal description overlaid? There's lots of work being done on that.

For me, specifically, what we're interested in is that intersection between how emotions and emotional states, as they're defined ... How do they intersect with a physical ... almost a stimulus? A burn or a cut, or maybe a chemical stimulus, or a mechanical is the general way that one experiences pain from the environment. How does the processing of those inputs ... ? How is that influenced when the brain's in a different emotional state?

Because this is very, very, important, again, for the clinical condition where comorbid problems related to, particularly, depression and anxiety are really dominant in the chronic pain state. We really do need to understand what the consequence of that double-whammy, if you like, is on that person's pain experience. Again, because that can help us more probably guide where we need to treat and fix all these different bits that have gone wrong.

Bill Glovin: I don't know if there's been an opioid explosion in Europe, but there certainly has been one in the United States. First, are doctors trained properly to prescribe opiates for different kinds of pain, and second, is there a way a doctor or a patient can gauge whether opiate use is appropriate for the level of pain they're experiencing?

Irene Tracey: That's a really great question.

I mean, I'm not a clinician, so my answers will be restricted to what I've observed as a pain scientist very much involved, doing some work looking at how opioids produce their analgesic state, and how different people have different analgesia to the same opioid, so what makes somebody have good analgesia and one person not.

Certainly, I think Europe and certainly Britain has watched with great interest what's happened in America, in the context of the opioid explosion, and very rapidly learnt from that. We have this government agency, NICE, and our British Pain Society very, very, active in communicating to our general practitioners,

which is the equivalent to your primary care physicians, what has happened over there and, again, strong advice and guidelines around opioid prescribing.

Whilst we were having a growing problem, I believe it's been very much nipped in the bud, and very clear guidelines have been put about the consequences and the negative consequences of, again, high-dose, long-term use. That, I think, having been a bad news story is now becoming a better news story. Certainly over here.

I think, again, going forwards, what we need to do, as you hinted at, is better education for all parties, both for the patient and for the physicians; for our young doctors being trained. I think very clear guidelines around their use, and more appropriate selection of which patients will benefit better and not. And again, terms of use, and what the longer-term consequences of being on particular doses of opioids, and what the consequences are on the body. Again, these are all ...

In fact, we are now actively involved with ourselves, so that we can contribute some data to this very, very, important topic. We hope that the next couple of years will have clarity on issues related to, what are the long-term consequences on the brain and other parts of the body of being on long-term opioids? Whether that, then, should guide maintaining a very short use of them only ever.

Also, we've been doing work characterizing, ahead of even going onto an opioid-based therapy, who's likely to have good analgesia to an opioid versus not very good. In which case, don't put them on an opioid-based medication, because it's not going to work for them. Again, it's early days yet, but we're starting to see signals that might be able to help us, what we call, personalize or stratify patients ahead and predict who's likely to have a good and who's like not to have a good outcome. In which case, there's no point in putting somebody on a treatment if that's not going to work for them.

This is not just for opioids; this is for all of our medications around pain. It's a big push right now is to do the more patient stratification, creative ways of using different tools, not just imaging, to characterize the patients and find out, "Okay, well, I think, for you, it should be this type of therapy, but for you, it should be this one," so that we can get people, one, onto their right therapy that's going to work for them, and we're doing that as early as possible, so that we can really reign in this chronic pain as quickly as possible as bring it down.

Bill Glovin: Great stuff. Are you finding that there's more student interest in specializing in this field? Is it a growing field in your estimation, and is there enough funding going on?

Irene Tracey: Well, again, those are great questions, Bill.

We are very fortunate to have some absolutely fantastic people in the pain field and great scientists and clinicians working in it, but we always want more. I think all disciplines would give the same answer, but what sometimes you need in a field, particularly to really shake it up and do a big paradigm shift and bring in some new ideas and fresh blood, is to get people who have been working in other areas to come in and take on this problem without any of the preconceptions of theories and things, and just come in with a fresh set of ideas.

I do encourage any young budding scientist out there, or clinician, if they've not thought about pain, to think about it because it is an absolutely, incredibly fascinating topic. There is plenty, as I hope they recognize, of interest in it from the pure science, the philosophy, and the chemical perspective, to get your teeth into. There's many, many, unanswered questions, so there's a whole career's worth there, so certainly, I would like to encourage people to come in. I think people coming who are, again, willing to be creative and challenge the dogma and the way we're thinking about it are to be welcomed.

In terms of funding, I think it is fair to say pain ... Because people don't die of pain, it's been this slightly orphan area in terms of politicization of it and funding of it. That's something that, again, all countries like the US and certainly the UK and in Europe, France, and Germany, there's many other countries, we've been very active with our societies to raise the profile of pain. Have global pain days focusing on different conditions to get the politicians interested, because the enormity of it.

I think people just didn't realize. One in five of the adult population have it. It's $600 billion a year in the US lost income. People not going to work because of pain, and treatment and management are €200 billion in Europe. This is a huge financial burden. It's a huge suffering burden.

I think those facts and that data, which some of the societies have done now and audited and pulled together, are very powerful pieces of data to communicate to our governments and our government funding agencies that this is a really big problem for society and we haven't addressed it with the level of funding that should've maybe been prioritized for it. We do need to raise the profile more.

It's certainly better, I'd say, these last years than it had been when I started 20 years ago, but much more work to be done for sure.

Bill Glovin: I think that's a great note to end on, Dr. Tracey. I know you have to go pick up one of your children-

Irene Tracey: I do.

Bill Glovin: So, I'm going to let you go. And again, tremendous work on the article.

Irene Tracey: Thank you.

Bill Glovin: Thanks for explaining all this to us and being so patient. Good luck with your research going forward.

Irene Tracey: Well, thank you very much, Bill. I'd like to thank the Dana Foundation for their support, and congratulate them on the wonderful way they communicate the excitement of neuroscience to society. It's great work that you're doing, so good luck to you, too.

Bill Glovin: Okay, thank you very much. Have a good day.

Irene Tracey: Okay. Bye now.

Bill Glovin: Bye.

That wraps up another Cerebrum podcast for this month. Thanks for listening. Remember to go to dana.org to find Dr. Tracey's article, and for all the latest news and information on brain research. Thanks for listening.