Airing Pain 112: Measuring Pain, Reading the Brain

How pain's subjectivity makes it difficult to measure, rewiring the brain and new research that allows patients to visualise their pain

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*In this edition of **Airing Pain**, returning contributor Mark Johnson, Director of the Centre for Pain Research at Leeds Beckett University, speaks to Paul about the experimental methods used in their lab to measure how pain is experienced. Professor Johnson emphasises the difficulty in communicating one's pain, as it is entirely context-driven and based on the experiences of the patient.*

Paul then heads to Manchester University to speak to Professor of Neuro-Rheumatology Anthony Jones. Paul learns about the different techniques used to measure the alpha waves produced by the brain when pain occurs, how the anticipation of pain is as important as pain itself and the difficulties that scientists encounter when trying to emulate these signals. We also hear about the brain's 'plasticity' – its ability to rewire connection based on sensory experience.

Anthony's research team are developing a 'smart neuro-therapies' platform (which you can get involved in, see 'More Information' below), a way for patients to measure their brain's alpha waves, which are important in controlling sensory experiences. The research could have significant implications in pain management. The team are employing a unique collaborative theatre piece, Pain, the Brain and a Little Bit of Magic*, to help patients, healthcare professionals, and the public to understand these complex systems.*

Paul Evans: This is ***Airing Pain***, the programme brought to you by Pain Concern, the UK charity that provides information and support for those of us living with pain and for health care professionals. I'm Paul Evans and this edition of ***Airing Pain*** has been funded by the Plum Foundation.

Mark Johnson: I'm a pain scientist, I've been in the field for well over 20 years. And the longer I'm in the field, the more I become uncertain about how we try to document pain in research settings.

Evans: How do researchers measure something as subjective as pain? On a standard pain rating scale, that is where zero is no pain and ten is extreme pain, someone might rate today's pain at eight, but a much better, more bearable five the following day. It might be the same *level* of pain, but the experience of it is different. Mark Johnson is Professor of Pain and Analgesia at Leeds Beckett University. He's also director of its Centre for Pain Research.

Johnson: One of the things we do in our lab is to use experimental pain techniques that are, in the main, non-injurious. So these are what we would call transient, temporary interventions whereby, for example, we might press a pressure probe on to the skin and keep pressing it until the person says that it's become painful. And then we measure the pressure that it took for the person to first experience the pain from the pressure probe, and we call that pain threshold. But as soon as you remove the probe, then the person's pain disappears, pretty much immediately.

Our other techniques involve, for example, plunging a hand into a bucket of icy water, and the person has to keep the hand in the water, tell us when they first feel the experience of pain, which we measure as pain threshold, and then we may well ask them to keep their hand in the bucket as long as they possibly can. And to take it out when they can no longer bear the pain from the ice water. And when they take their hand out, then we measure that time as the time-to-pain tolerance. And of course, when they take their hand out, then the pain starts to disappear quite, quite rapidly, and there's no lasting damage from that type of technique.

Evans: It's quite interesting because pain is subjective, and even from a day to day point of view, pain is different. I can remember being asked for years and years ‘Are you in pain?’ and you say ‘No, I'm not in pain, I'm aching’, but aching is pain.

Johnson: Yeah, yeah. Pain is exactly what the person says it is. Pain is subjective. So we've got no objective measure of pain. There's no probe that we can put on somebody that will identify that that person is or is not in pain. So as a consequence, pain is very much about a person's ability to communicate their sensory experience, the sensations that they're feeling at that moment in time. For them to do that is really all about when they decide to use particular words to describe those sensations. Whether it's an ache or a pain is really determined by that person and

the context in which the question has been asked.

I've always been concerned about scaling pain. Often patients are asked ‘Can you tell me on a scale of one to ten, how much pain you're in at this moment in time? Where one's minimal pain and ten’s the worst pain imaginable?’ And that's actually quite hard to do. I don't convert my pain into numbers.

Evans: It's very difficult.

Johnson: Absolutely. And there's a little bit of an assumption that that scale is linear. Certainly, we know that if you compare somebody's pain intensity rating of five with somebody else's pain intensity rating of five, you cannot say that those two people are experiencing the same intensity of pain, because pain is personal to them.

I prefer using scales that are more descriptive. My pain’s moderate, my pain’s severe, my pain’s mild. I think you get a better insight into what the person is experiencing when they're using those sorts of terms.

And yes, when do you convert an ache into the sensation of pain? Well, again, it's the context. If you're in a pain clinic, and you're trying to explain to a physician, for example, that you're experiencing something that is really quite distressing, you might use the word pain. But if you're in a, I don't know, a social setting, you might just use the word ache. So pain’s very much dependent on the context in which you're expressing it.

Evans: So what sort of experiments are you doing in here?

Johnson: We've got two main themes. We look at factors influencing an individual's response to a noxious stimuli. We call it pain sensitivity response and that's things like the age of the person, the gender, the sex of the person, ethnicity, and body fat composition, for example. So that's one strand that we look at. And another strand is the factors that influence a person's response to treatments, mostly non-pharmacological treatments. I'm particularly interested in TENS, acupuncture, things like kinesiology taping.

Evans: What sort of results have you found?

Johnson: With respect to the factors influencing individual response to noxious stimuli, painful stimuli, we found that gender role does seem to have an influence. So it's well-established in the field that the pain threshold of women tends to be lower than the pain threshold of men. And there's been a debate of whether that's just that women are more likely to report pain more readily than men, or not.

Animal studies suggest that actually, there's a biological underpinning to that finding. In our studies, we have found exactly the same, that women express pain more readily than men in laboratory settings and that their pain threshold and pain tolerances are lower than men.

And what's quite interesting about our work is that we found that that seems to link into what's called gender role. It's a societal view and in certain societies, that men need to be tough. For example, they need to be able to withstand pain and situations in which they're experiencing pain. We're finding that that sort of plays out in the studies that we've been doing in the lab. And that seems to go across culture as well. We do quite a lot of work on people from Arab countries, from the Middle Eastern, North African countries. We found that that gender role seems to play across into those cultural settings as well.

Evans: Some people might be surprised that women's pain threshold is lower than men. Particularly in the UK, where we have this thing called man flu, just anything will send us to bed in agony, whereas women carry on.

Johnson: Yeah, but as I said earlier, pain's all context-driven. So I think it's the context in which you're expressing how you feel. So in a laboratory setting, the subjects *do* know that it's an experiment that will be comparing men against women. So I think there's a whole load of factors that play out in that setting.

Men will express their man flu more readily, perhaps in a societal setting because they're wanting sympathy from their wives, their partners, their friendship group. Men tend to not express (I find being a cyclist), those sorts of ailments as much when they're with their fellow sporting colleagues. Now I've got no research to back that up. But I think it's just that idea that context really drives the way that we express how we feel.

Evans: Men maybe don't want to show other men that they're in pain, the alpha male of the group and things like that, I suppose.

Johnson: Yeah, yeah, yeah. I think there have been studies done but they've looked at these sorts of settings where you're doing, say, the cold plunge experiment. When there's been a female observer and a man participant, and a man observer and a man participant and playing that dynamic out, the investigator's gender and sex is also quite important, I think.

Evans: Professor Mark Johnson, director of the Centre for Pain Research at Leeds Beckett University.

So there are many variables to take into account when one is measuring pain. Wouldn't some form of diagnostic readout like we have in the motor industry be very handy?

Anthony Jones is Professor of Neuro-Rheumatology at Manchester University where he leads the Human Pain Research Group.

Anthony Jones: We call all the different ways of trying to get a readout of what the brain is doing 'functional brain imaging'. So that's just a collective term for different types of ways of measuring what the brain is doing. There are a number of different techniques. Electroencephalography, which we use a lot, which is recording electrical signals on the surface of the scalp. So this is a non-invasive technique and that's able to pick up conversations that are going on in the surface of the brain.

Evans: Hang on, now, what do you mean [by] 'conversations that are going on in the brain?'

Jones: The way that the brain communicates with itself, and different parts of the brain, is through sending electrical signals and receiving electrical signals to different parts. So, if you imagine a huge number of circuits, some very small, some very extensive, all communicating with each other at the same time. Of course, many regions of the brain are doing many different things, and doing some of those things at the same time. So it's a very complex organ to try to understand.

Evans: So the brain is talking to itself, if you like, or different parts of the brain are

talking to itself?

Jones: Yes.

Evans: Is there a point in the brain that is purely involved in pain? Is there a pain centre in the brain?

Jones: Well, that's a really interesting question and it's preoccupied neuroscientists for many decades, if not a century, and the conclusion has to be no, there isn't a single pain centre. In fact, this is one of the pieces of work that we did right at the beginning of my career when we were the first group to use a technique called positron emission tomography, which is a way of measuring blood flow, and other chemical changes in the brain.

Before the advent of functional brain imaging techniques, the only way you could access how the brain might be responding to pain was actually by sticking electrodes or stimulating different bits of the brain during neurosurgical procedures when people have to be conscious, awake, because you need to know whether you're interfering with functionally essential bits of the brain.

So there's a number of neurosurgeons, mainly in Canada, who are very painstakingly either stimulating different bits of the surface of the brain, or sometimes recording as well and they had real difficulty eliciting pain at all by stimulating different bits of the surface.

[During the] 50s and 60s there was a great interest in psychosurgery, so chopping out different bits of the brain. So there was a great vogue for people with very serious depression and other psychiatric problems, cutting out, chopping out bits of the frontal cortex (so the front of the brain). That obviously had a fairly major effect on people's personality and motivation. So they started chopping out or chopping the connections to a bit of the frontal cortex, which is the more emotional bit of the frontal cortex called the cingulate cortex. When they did that patients still felt pain, so they were able to register pain, but it no longer bothered them.

Evans: So you're taking the emotion away from the pain?

Jones: Exactly. And that was the sort of first indication that perhaps the sensory, so

the ‘Where is it?’ and the ‘When is it?’ aspects of pain might be processed separately to the emotional aspects of pain.

Evans: An example that lots of people use is that if you stamp on my foot, and I’ve just won the lottery, I don't mind the pain, the pain is okay. But if you stamp on my foot and something really bad has happened to me, I really feel the pain.

Jones: Absolutely. The one thing that we've learned from three decades of functional brain imaging is that the experience of pain is a highly variable, highly plastic process that is very context-dependent. So we're really talking about the psychological context, which is what you were just mentioning.

A beautiful example of that is the placebo effect, which is really the ability to experience something completely differently. Not because of anything physical, just because of a verbal or visual cue about what you might be about to experience. This is why we can be hopeful about pain because it's all processed in the brain. The brain is a very powerful organ and we can actually change the way it's processed, so there is this plasticity.

When you experience pain, there's lots of different components to that. There's the actual stimulus that might be painful, so sticking a needle in the skin or moving a painful joint. But there's also all the things around that. So there's the expectation or the anticipation for that stimulus or that experience. There's also what comes afterwards, so how you respond to that. Is it going to stop you moving or is it going to make you move faster?

We’re built to – or designed to – respond in different ways to pain under different circumstances. So if you're anticipating pain caused by a nasty animal that might kill you, well, you're going to have a very different response to that [than] to anticipating pain that might come from a painful joint. You can interrogate that in a laboratory and look at how the brain responds both to the anticipation of pain and to the actual pain itself. What we've learned from studying that over the last few years, is that the anticipation of pain is almost as important as the actual stimulus that causes the pain, in terms of informing the experience that we actually have.

Evans: But for those who have chronic pain, permanent pain, there's no anticipation

involved, we *know* that we're going to hurt tomorrow. So how does the brain react to that?

Jones: You say there's no anticipation, but there will *always* be anticipation because you're always projecting what you might be experiencing into the future. In fact, a large part of our brain is geared to *just* planning for the future, particularly the front of the brain, the frontal cortex is very involved in memory. So remembering what happened before, projecting what might be happening in the future and integrating those things into a current experience.

The brain has this job of interpreting actual sensory experiences, but also integrating that with previous experience. It's juggling the actual sensory input, if you like, the here and now, with what's happened before, and how that might affect the current experience. So the brain, in that sense, is doing a kind of virtual reality job on how we feel.

In some people, their pain may be *more* driven by what they're expecting than the actual sensory input. Other people may be much more driven by just the sensory input and less influenced by what they're expecting. So what we've found in patients with different types of chronic pain, including fibromyalgia and osteoarthritis, is that there's a fine-tuning problem in the brain in the way they do that integration, such that people with chronic pain are tending to anticipate more. So there's more processing of that, expectations in certain bits of the brain, particularly in a small island of cortex, called the insular cortex. That increased expectation correlates very nicely with the extent of their symptoms, so how extensive and severe the pain is. Whereas the bits of the brain that are concerned with controlling those responses in the frontal cortex are *less* active and that correlates very nicely with *less* good coping strategies. By that, I mean, the tendency to think things are going to be terrible ‘Oh, my God, it’s all going to be ghastly’, so what we call catastrophising.

Evans: So the big question is, you talked about plasticity of the brain, that's the brain's ability, if you like, tell me if I'm wrong, to rewire itself. How do you rewire the brain or can you rewire the brain?

Jones: Well, that's a really good question that we don't really know the answer to. We know the brain can rewire itself in terms of remaking connections. If the brain is

damaged, it can remake connections, although we don't really understand that process very well. That's very important to patients who have chronic pain as a result of damage to the brain, such as patients who have post-stroke pain, for instance.

But it can also virtually rewire itself by just changing the strength of those connections in the brain. One very famous example of that is if you look at London taxi drivers. The bit of the brain called the hippocampus, which is concerned with learning about spatial things, such as streets and where streets are, is bigger than normal. If they stop driving taxis or stop learning about driving taxis, then that changes and it goes back towards the normal. So the brain is continuously changing in that way, reinforcing connections for some things, reducing the strength of those connections for other things. That's what we call plasticity.

Evans: So if we know that we are catastrophising, that the worst is going to happen, 'I'm going to get up this morning, and it's going to be absolutely grim'. If you could change the way, or if I could change the way I think about things. I wake up in the morning and the sun is going to be shining and why should I catastrophise in the first place, that might rewire a little bit of my brain to make me feel less pain?

Jones: Yes, and there is some quite good evidence that happens both functionally and structurally. A few years ago, we looked at the effects of a kind of cognitive therapy or talking therapy called mindfulness-based cognitive therapy. We found that if patients just got a short course, so an eight-week course, of this kind of therapy, these fine tuning problems that we've discovered in the brain could be partially, not completely, but very substantially improved.

Functionally, we know we can change and those changes, correlated with reductions in the unpleasantness of the pain, but we also know that structurally similar things can occur, and that they can also be reversed. So a number of people, including researchers in Oxford, have found changes in the structure of the brain in relation to the grey and the white matter and that, if the pain improves, then some of those structural changes can be reversed. So again, it's this idea that although chronic pain is difficult to treat, a lot of the processes that seem to be important in perseverating that pain are actually, or potentially reversible.

Evans: That's Professor Anthony Jones, who is Professor of Neuro-Rheumatology

and leader of the Human Pain Research Group at Manchester University. The group are still looking for volunteers. Volunteers, that is, who have chronic pain, and those who don't have chronic pain, to take part in their study to develop and test a therapy for chronic pain that increases pain resilience. For more information, just check out their website, which is research.bmh.manchester.ac.uk/pain and look for the drop-down link that says 'Want to volunteer?' Now if that's all too much to remember, just contact Pain Concern and we will put you in touch.

I just need to remind you that whilst we in Pain Concern believe information and opinions on ***Airing Pain*** are accurate and sound, based on the best judgements available, you should always consult your health professional on any matter relating to your health and well-being. He or she is the only person who knows you, your circumstances and therefore the appropriate action to take on your behalf. You can download all editions of ***Airing Pain*** from Pain Concern's website, which is painconcern.org.uk, where you will also find a wealth of material and information about living with and managing chronic pain, including our newly developed Navigator Tool to make consultations between you and your doctor much more effective.

Now, creating greater understanding of pain is at the heart of what we do at Pain Concern and bridging a communication gap, perceived or otherwise, between patients and healthcare professionals, is something that more and more doctors and researchers are trying to do. No more ivory towers where, in days of yore (well, hopefully anyway), patient involvement wasn't seen as part of the medical solution. And, in that spirit, Professor Anthony Jones uses the power of public performance for chronic pain sufferers and the people who support them, medical professionals and absolutely anybody who wants to know more about what makes the brain tick. In his show *Pain, the Brain and a Little Bit of Magic*, he collaborates with Naive Theatre Company, using poetry, music and a bit of stand-up and an oversized interactive model of the brain, to bring what's described as an optimistic message of how chronic pain may be better understood and treated.

Jones: We thought of it originally as just a way of bridging the knowledge gap. But now we're thinking about it a little bit differently, and perhaps a way to really bring together the pain community and all the people that are involved in that. So what's

made us think about that a little bit more is that we're now developing some new brain-based therapies to treat chronic pain more effectively. So we're doing that in quite close collaboration with our patients. We're now thinking actually that *Pain, the Brain and a Little Bit of Magic* could not just be a vehicle for explaining about that, but actually as a kind of catalyst for bringing these groups together in a sort of collaborative way.

Evans: What sort of therapies are you developing from this then?

Jones: Mainly based on the work we've done over the last three decades. We've done a lot work on experimental placebo, and discovered doing that process that when we're expecting to have a positive response from a placebo intervention, the brain expresses more alpha waves, particularly in the frontal and insular cortex. We didn't really know what that meant, then one of our PhD students, Kathy Ecsy, did a whole PhD on whether this was important or not. And she did that by applying an alpha rhythm to either a visual or auditory stimulus. To cut a long story short, we found that if you do that, you get a painkilling effect on normal volunteers.

Evans: Let me see if I can get this right. There are alpha waves involved in a particular stage of sleep and they are the restorative, the healing waves, if you like. Sometimes, (you must tell me if I'm wrong here), sometimes those alpha waves are missing in sleep?

Jones: We don't really know exactly what the role of all these different waves, including alpha waves, are in sleep. But certainly alpha waves are associated with sort of early stages of relaxation and, as you say, restorative sleep. We know that patients with chronic pain particularly complain about poor sleep [but] we don't really know what the relationship is between the sleep and the chronic pain. Some of my colleagues think that it's the poor sleep that generates the chronic pain. The nub of it is, we don't really know.

There is also quite a lot of evidence from other sources that alpha waves may be important in controlling aspects of sensory experience. What we now think is that alpha is probably quite important in the kind of top-down control of how we feel. So we're developing a platform. It's a technical platform and the idea is that patients will be able to use this in their own home. The actual platform will be downloaded on

either a laptop or their smartphone. They will also have an individualised EEG cap, which they'll be able to just plonk on their head. Because there'll be wireless communication between their smartphone and their brain, they'll be able to see how much alpha they're expressing in their brain. If they look on their pain diary, and they notice their pain is pretty bad, has really been getting worse and worse in recent times, then they might decide to engage with a number of options, which will be available on this pain platform.

At the moment, the two main options are one probably more for acute, so recurrent acute pain that a lot of these patients experience. They'll be able to plug into an alpha entrainment programme that will just allow them to experience alpha either visually or with an auditory input. They will choose how long they want to engage with that, probably twenty minutes at a time. So if they’re getting particularly bad pain that's interrupting their reading or watching television or whatever, they've got something that they can engage with for a short period of time. So we're just testing out whether that actually works for chronic pain patients at the moment.

The other aspect is to try and train the brain in a more long-term fashion to express more alpha. With that, they'll be able to look at what's going on in their brain on their smartphone again, and then train themselves to actually express more alpha waves themselves over a period of weeks or months. We've got ideas about kind of doing more sophisticated things beyond that. So it's a kind of generic platform that allows us to allow patients to interact with their brains in a positive way.

Contributors:

- Professor Mark Johnson, Professor of Pain and Analgesia and Director of the Centre for Pain Research, Leeds Beckett University
- Professor Anthony Jones, Professor of Neuro-Rheumatology at Manchester University, Human Pain Research Group Lead, creator of *Pain, the Brain, and a Little Bit of Magic*.

More information:

- University of Manchester neurofeedback study volunteering: research.bmh.manchester.ac.uk/pain/ and click the 'Want to Volunteer?' tab at the top of the page
- *Pain, the Brain, and a Little Bit of Magic*: manchester.ac.uk/discover/news/pain-the-brain-and-a-little-bit-of-magic-as-research-goes-from-lab-to-stage/.

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