# Episode 4 - Prof. Ralf Baron - Living with Fire Patients Tell Their DPN Stories

### Speaker 1

Welcome back to Inside the Silent Storm. I'm D. Lim. And today we're shifting our focus from mechanisms to the patient experience with diabetic peripheral neuropathy. Over the past three episodes, we have explored the global impact of diabetic peripheral neuropathy as cellular mechanisms and the nature of neuropathic pain. And the research in this domain matters. Early detection is crucial, and we must never lose sight of the healthcare practitioners behind the diagnosis.

#### Speaker 1

These narratives of burning sensations, sleepless nights, and the struggle to maintain normalcy will be balanced with stories of resilience, hope, and community support. Joining me today is Professor Ralf Baron, an expert in the neurological mechanisms underlying complications among people with diabetes. Professor Baron is the head of neurological pain research and therapy at the University of Kiel in Germany. A global expert in neuropathic pain served in the leadership roles within IASP, NeupSIG, and German Pain societies.

## Speaker 1

We will explore the fascinating and troubling world of how hyperglycemia damages our peripheral nerves, and why recognizing these early signs is so crucial. Joining me to provide clinical context for these patient experiences is Professor Ralf Baron, who will help us understand the neurobiological basis of what our patients describe. Professor Baron, could you please briefly summarize how the pathophysiology a diabetic peripheral neuropathy could actually bring about the sensation of fire or the pain that our patients commonly describe?

## Speaker 2

So a pain is, the classical positive symptom of neuropathies and the in particular the burning quality of the pain. The burning sensation is today linked to a different and very specific receptor on the pain fibers on the nociceptive C fibres. So we have learned from many, many studies and particular studies in skin biopsies by labeling these fibers and that even in patients, that the upregulation of the capsaicin, the so-called capsaicin receptor on pain fibers, will lead to the burning sensation.

## Speaker 2

And for example, another, channel which is the sodium channel is also upregulated due to the damage of the neurons in diabetic neuropathy. This upregulation will lead to the shooting pain. Some patients, perceive.

### Speaker 1

So is there any way for for the patients or even the managing physician to understand what is the distribution of these different types of, receptors or fibers? Is there any way, apart from doing the skin biopsy.

## Speaker 2

To assess these upregulation? Again, this is difficult. Skin biopsy is the only way to really directly label them and to see them. But as we know that the burning sensation is associated with the upregulation. So it's very logical that burning will be an indicator of upregulation of TRPVI capsaicin receptors.

### Speaker 1

Okay. Then some comments from the patients during the clinic consults, they say, hey, my pain will only occur at night, and I might have sleepless nights because of this pain. Is it true?

Speaker 2

Yeah. That's, absolutely true. And perhaps for the explanation, you have to realize that these specific fiber, channels, these, receptors, the TRPVI receptors, the capsaicin receptors, they are normally, on warm fibers on our normal physiologic warm fibers. So this is our trend structure for warm sensation. And under the pathophysiological conditions of a neuropathy, for example, diabetic neuropathy, they appear on pain fibers.

Speaker 2

And that means that every warm stimulus will now induce a pain fiber and will activate the pain fiber and induce pain. A painful sensation. And in particular, during the night, under the blanket, for example, the feet are warmer than normal and then the warmth of the night will activate pain fibers, and this will induce this burning pain sensation.

Speaker 2

This is the reason for the night pain of all patients.

Speaker 1

So is it the same as the restless leg syndrome?

Speaker 2

Well, restless leg syndrome is a little different. It might be associated with polyneuropathies, but in this particular case, there's an urge of the patients to use their feet to walk to get relief of the symptoms. And this is, in the burning and classical burning case, not necessarily the case. So there's a difference between restless legs and spontaneous burning phenomenon, okay.

### Speaker 1

And that's the reason why that we always say you need to do as many tests as possible, to, from different types of the pain fibers in order to delineate what would be the stages of diabetic peripheral neuropathy and which fibers are actually being affected for that person sitting in front of you in the clinic. Yes. So, Professor Baron, in your opinion, for people living diabetic, peripheral neuropathy is just is it just about the neuropathic pain per se?

#### Speaker 1

Do they have other problems?

### Speaker 2

Well, the neuropathic pain is a predominant problem. But chronic pain will always be associated with co-morbidities. And these comorbidities are depression, anxiety, sleep disturbances. So we talked about the problems during the night. And there are lots of studies clearly showing that neuropathic pain is much more frequently associated with these comorbidities. As nociceptive pain states, although the pain intensity might be exactly the same.

#### Speaker 1

So is it just because of the pain that arises due to underlying diabetes condition would have led to this association with anxiety, depression, or is actually some, changes in the brain region?

#### Speaker 2

Yes. Absolutely correct. There are some brain regions which are particularly activated in neuropathic pain states. There is the prefrontal area in the brain and the anterior cingulate area, for example. And exactly these, are associated with the comorbidities we are discussing at the moment. So there is plasticity in the brain in these affective areas, that, yeah, lead to the co-morbidities in neuropathic pain states.

### Speaker 1

I mean, does it mean that if you want to scan the brain, then you may see a different light up of that? Affected region, which may have a close association with the intensity of the pain and intensity of the mental health condition.

#### Speaker 2

Yeah. Absolutely correct. So in particular, there are very nice animal trials showing that the connections between these different brain areas, anterior cingulate cortex, for example, and others, associated with hyperalgesia. So one phenomenon of diabetic neuropathy. So this is correct. There's a clear association of the brain activity in these areas and the pain intensity in all patients.

#### Speaker 1

Then are we are we currently practicing, having some brain imaging to delineate the intensity of pain? Yes. Well.

## Speaker 2

On the research level you could you will see this, but for practical issues, I think it's not doable. Yeah.

### Speaker 1

Okay. So far we are yet to, to have that. And how are we going to help our patient to cope with the anxiety and depression.

### Speaker 2

Well we can use psychological strategies like coping strategies and so forth and reduce these plasticity changes in the brain which are associated with the pain. So this is one approach to do. And I think psychological support is always important. And in chronic pain patients. But we also can use medications for example, which on one hand will effect the pain system and reduce the pain, but also has a good effective beneficial effect on comorbidities like anxiety, sleep problems and depression.

### Speaker 1

Thank you very much, Professor Baron. I've learned so much today.

### Speaker 2

Thank you.

### Speaker 1

To this episode has been perhaps the most moving of our series so far. Professor Baron, thank you for helping us understand the scientific rationale behind this very human experiences. What

is remarkable is how the patient descriptions align perfectly with what we know about the physiology of diabetic peripheral neuropathy. The stories we have heard today remind us that diabetic peripheral neuropathy is not just a footnote in diabetes care.

#### Speaker 1

It a life changing condition that affects every aspect of the person's existence, from the simple act of walking to the complex challenge of maintaining relationship. Diabetic peripheral neuropathy touches everything. But what gives me hope, and what I hope our listeners take away is an incredible resilience of the human spirit. Despite facing daily challenges that many of us can barely imagine, these individuals continue to fight, to adapt and to find meaning and joy in their lives.

### Speaker 1

For healthcare providers, listening to these stories should remind us to always ask our patients, not just about their glucose level or medication adherence, but about their pain, their sleep, their fears, and their hopes. In our next episode, we will explore the fight against pain, latest treatment and innovations, where we will discuss both established and emerging treatments that offer hope for better pain management and improve quality of life.

#### Speaker 1

Thank you for joining us today. As we listen to these powerful voices from inside the Silent Storm. Thank you for joining us on this journey. And remember, in the fight against diabetic peripheral neuropathy, knowledge truly is power. Until next time, take care of yourself and each other.