MIGRAINE WORLD SUMMIT

TRANSCRIPT

INTERVIEWS WITH WORLD-LEADING EXPERTS

HOW MIGRAINE & CHRONIC FATIGUE SYNDROME (ME/CFS) ARE CONNECTED

JAMES BARANIUK, MD
PROFESSOR
GEORGETOWN UNIVERSITY

Introduction (00:05): Another situation where that's just very important is when you have a good day and you feel like you can do anything, and you go out and you try to do everything. And what happens is you rebound, you have the post-exertional malaise, and then boom, you're worse than you were before. You have to limit yourself. Don't try to do too much. This pacing is very, very important.

Lisa Horwitz (00:35)**:** Brain fog, extreme exhaustion, poor sleep, and dizziness are known symptoms of migraine, but they're also symptoms of myalgic encephalomyelitis (ME), known as chronic fatigue syndrome (CFS). Many people who live with chronic fatigue syndrome also experience headache or migraine. This talk will explore the correlation between ME/CFS and migraine. We are honored to have the director of the Chronic Pain and Fatigue Research Center at Georgetown University, Dr. James Baraniuk, to guide the way. Dr. Baraniuk, welcome to the Migraine World Summit.

Dr. Baraniuk (01:11)**:** Hello.

Lisa Horwitz (01:12)**:** All right, we have a lot to cover, so I'm going to just dive right in. What is myalgic encephalomyelitis, or chronic fatigue syndrome?

Dr. Baraniuk (01:23)**:** This is a disabling severe disorder where fatigue is the predominant feature, but another aspect that's important for diagnosis is to have post-exertional malaise, abbreviated as PEM. The fatigue should be present for six months and disabling so that a person can't do their usual activities. The post-exertional malaise refers to what happens after somebody does more exertion than usual, such as more physical work or cognitive, even emotional stress. They find that their symptoms all relapse and become very significantly worse, and this often has a delayed time course, so that 24 hours after the stressor, they are unable to do their usual amount of work.

Lisa Horwitz (02:25)**:** Now, is ME/CFS something that is diagnosed through lab work or tests?

Dr. Baraniuk (02:31)**:** The diagnosis can be a little bit complicated. There are several standard criteria that are used, and they're all based on symptoms, but again, you have to have the disabling fatigue, post-exertional malaise, sleep disturbances, and then problems such as cognition, brain fog, or orthostatic intolerance, which is — the orthostatic problems are when you stand up, you get dizzy, lightheaded, and may actually have a very fast heart rate.

Lisa Horwitz (03:14)**:** So, blood pressure, kind of, regulation issues?

Dr. Baraniuk (03:18)**:** Well, it's not necessarily blood pressure. Usually, if someone has an orthostatic problem with blood pressure, they stand up, and the blood pressure will drop. That's orthostatic hypotension. But in CFS, it's more postural orthostatic tachycardia syndrome, or POTS, where you stand up and now your heart rate will go up by 30 beats compared to when you're lying down. And this is often underappreciated. It's often not asked by doctors during their history or tested. And that's important because it's relatively easy to do what's called the NASA stress test, or NASA Lean Test, rather. In the doctor's office, you would stand with your back against a wall, your feet about 10 inches away from the wall, and you stand there for 10 minutes, having your heart rate and blood pressure taken every minute. And what's found is that by the third, fourth, towards the 10th minute, people with POTS will have their heart rates jump significantly — by greater than 30 beats compared to lying down.

Dr. Baraniuk (04:40)**:** We have some laboratory tests that we think are very good at identifying people with ME/CFS, but they're just not ready for widespread use. As far as treatment, it can be very frustrating because there is no FDA-approved medication or therapy for ME/CFS. The treatment generally begins by making the correct diagnosis. To do that, the doctor has to evaluate and make sure that there are not other illnesses that could be causing the same types of symptoms. For example, [you] could have congestive heart failure or thyroid disease. After you've made those necessary exclusions, that plus the normal blood tests, the pattern of symptoms leads you to the diagnosis of ME/CFS.

Lisa Horwitz (05:51)**:** Do you think that because there is no one test and there's such a broad range of symptoms that ME/CFS is underdiagnosed?

Dr. Baraniuk (06:00)**:** Absolutely. It's thought that perhaps we know of only a third of the people who meet these criteria. The other two-thirds may have symptoms, be disabled, be at home, and not have a diagnosis.

Lisa Horwitz (06:18)**:** Wow, that's a significant amount. Tying this into migraine, we know that there's a significant genetic component to migraine and headache disorders. What are thought to be the causes of ME/CFS? Are they genetic?

Dr. Baraniuk (06:36)**:** There is actually rather poor evidence for a genetic basis. Studies from a few years ago in twins suggested that about a third of the risk for developing ME/CFS could be inherited, but there seems to be a lot more room for environmental effects. These are probably related to getting virus infections [and] having other stressors that then lead to the full-blown symptoms of ME/CFS. There are studies ongoing right now to answer this in big groups like the [U.K.] Biobank, and I think we'll get better answers in a couple years.

Lisa Horwitz (07:27)**:** That's exciting. We know that ME/CFS affects more women than men at an approximate ratio of 4 to 1. Do hormones contribute to CFS?

Dr. Baraniuk (07:40)**:** This is an obvious thing, but it's only relatively recently that there have been studies suggesting differences in testosterone, estrogen, and other hormones that may contribute. Another contributing factor is that many of the people who developed this are in their 30s to 40s, which can cover the perimenopausal period, so it may not be an actual level of a hormone, but rather the change from being menstrually active to postmenopausal changes, and those in and of themselves are quite complex. The fact that it's a change in the hormone levels makes it also more difficult to come up with some sort of diagnostic test. I think it's more important to look at that time period, though, because it will contribute to making the appropriate diagnosis. And then also there are differences between men and women. In fact, we're trying to look at that right now. One of them is that women tend to be more tender [to pressure] than men, and this is particularly the case in women with fibromyalgia, where you used to use your thumb and pressure points to make a diagnosis. Now that's not done so much, but being tender to pressure seems to be a greater problem in women than it is in men. And that goes back to places in the brain stem that regulate the way that pain messages, other messages from your body are viewed, sorted, and allowed to travel up your brain to notify you as to what's happening in your body and around you.

Lisa Horwitz (09:41)**:** So you think the brain stem sensitization causes some of these symptoms?

Dr. Baraniuk (09:46)**:** Yes. In fact, it's called central sensitization. And I'm glad you brought that term up because the other words like hyperalgesia, systemic hyperalgesia, get to be more of a mouthful, but they generally suggest that changes in these filters that ordinarily would stop pain messages or other messages from, say, the intestinal tract, the filter doesn't work. So now the pain messages start to go through, and you perceive them and take actions to avoid the pain. That may cause some of the so-called sickness behaviors that can also occur in this and other diseases.

Lisa Horwitz (10:35)**:** So you've hypothesized that the central sensitization thought to be involved with migraine also plays a role in the pathophysiology of CFS. What implications does this have, though, for the treatment?

Dr. Baraniuk (10:50)**:** Well, I think it's very instructive. There are several very beneficial treatments for migraine, as you and your viewers realize, from the ergot alkaloids to topiramate to now intravenous monoclonal antibodies to calcitonin gene-related peptide (CGRP). I have tried to look at our patients to see if any of those affect the underlying symptoms of ME/CFS, as well as helping with migraine. And it's certainly clear that they are beneficial for migraine, and I'm not so sure that they do anything specifically for the CFS, but it's complicated because if you reduce a trigger such as severe headaches, then that's one improvement in their life that isn't going to lead to the post-exertional malaise, exertional exhaustion type of recurrence of all of the symptoms that I mentioned earlier. So overall, for a person who has migraine, I think it's very important that they take appropriate therapy, and that will help the overall situation with the ME/CFS.

Lisa Horwitz (12:20)**:** What percentage of people with ME/CFS also have migraine or headache?

Dr. Baraniuk (12:25)**:** The patients that we've seen, I use the International Headache [Society] criteria, and I find that up to two-thirds of my ME/CFS patients meet the criteria for migraine headaches. Most of those are migraine without aura, and, again, females may be more predisposed than males. This is difficult to compare to electronic health records, where you don't see that big risk of migraine in ME/CFS, but I think the real reason is that I'm asking every one of my patients about migraine and I'm able to make a diagnosis, and easily half of the people I see have never been asked about migraine or stigmata, like sound and light sensitivity or auras. And I think that it's very useful for the patients to bring it up with their physician so that an appropriate diagnosis of migraine can be made and appropriate treatment started.

Dr. Baraniuk (13:47)**:** One of the difficulties in the research area is, we tend to get in a silo. Many CFS people don't ask about migraine. Many migraine investigators don't ask about ME/CFS. And as a result, the two groups can't share their data, can't bring it together, and synthesize the bigger picture. Going forward, I think that's going to be very important, and I would suggest that the migraine investigators contact ME/CFS researchers to try to break down that barrier and understand what's the same between migraine and ME/CFS; migraine, ME/CFS, and long COVID; even with fibromyalgia, with the pain syndromes, so that we can share other aspects that will give us clues to the pathogenesis and an inkling of whether some of the medicines used in migraine may be beneficial in these other illnesses.

Dr. Baraniuk (14:56)**:** Recently, there's been felt to be an overlap between connective tissue disorders like Ehlers-Danlos syndrome with ME/CFS, with some investigators feeling that as many as half of their patients have this sort of peculiar type of connective-tissue problem. The Ehlers-Danlos people will tend to have very stretchable skin, be double-jointed, if you will — be able to move their joints, their thumbs, put their feet behind the back of their head in extreme cases — and there's something about this that may tie into the risks for ME/CFS. It's an open question right now, but something for people who do have the highly stretchable skin, for example, they may want to talk to a rheumatologist about it.

Lisa Horwitz (16:00)**:** For patients who have systemic body pain, and that includes their head, on a daily basis, how do they manage the pain without then inducing medication overuse headaches?

Dr. Baraniuk (16:15)**:** Very good question. If you have chronic widespread pain plus fatigue or sleep disturbance, you now meet the new criteria for fibromyalgia.

Lisa Horwitz (16:32)**:** Really?

Dr. Baraniuk (16:33)**:** Yes, there's been an evolution of the diagnostic criteria over the years with fibromyalgia, and if you've got chronic pain, then I'd suggest that you contact a rheumatologist or tell your primary care physician that you may meet the new criteria and therefore may be eligible for drugs such as the [pre]gabalin, that are non-opiate medications that do help with the chronic pain.

Lisa Horwitz (17:15)**:** So those types of medications are more geared towards patients with fibromyalgia. Are there medications that are used for patients with ME/CFS?

Dr. Baraniuk (17:25)**:** Yeah, if you've got chronic pain — chronic widespread pain — then I would say it overlaps with fibromyalgia, so use the drugs that are approved for fibromyalgia. If you've got migraine, use the drugs that are approved for migraine. If you have irritable bowel syndrome, use the dietary and other measures that are available for irritable bowel. If you have postural orthostatic tachycardia syndrome (POTS), then make sure you keep your fluid status well, keep hydrated, and if necessary, use the appropriate drugs that are standard in POTS. We're sort of grasping at straws here, but it means that if there's something of value from another field or one of these other syndromes, then we should incorporate it into the overall treatment plan for particular individuals with ME/CFS.

Lisa Horwitz (18:37)**:** Do you recommend to patients seeking relief to try to do a general systemic anti-inflammatory diet or other anti-inflammatory processes or procedures?

Dr. Baraniuk (18:50)**:** I think it's a reasonable thing to say, but it's very difficult to do, and to show that things like high doses of antioxidants, for example, would be of value so far hasn't seemed to work out.

Lisa Horwitz (19:09)**:** And I imagine that there is no known way to reduce inflammation within your brain.

Dr. Baraniuk (19:18)**:** Actually, there may be things that will be absorbed through your gut and then transferred across the blood-brain barrier, could be very effective because small chemicals and metabolites can readily cross into the brain.

Dr. Baraniuk (19:38)**:** This brings up another issue, which is that the energy factories, the mitochondria, appear to be defective in ME/CFS, and this may contribute to the sense of weakness or heaviness in the muscles but also contribute to poor function in the nerves themselves. For example, since neurons require a lot of energy through mitochondria to work, so that if we can provide some support for the mitochondria so they can generate energy more efficiently, we may get improvements, as well. There are a few supplements that have been used, such as N-acetyl cysteine, the carnitine lipids, CoQ10, that may serve a purpose there in making the mitochondria more efficient and so generating more energy throughout your body, and also being able to turn off some of the inflammatory signals, such as reactive oxygen species, which are very probably quite deleterious.

Lisa Horwitz (21:06)**:** So, since we know there's not a specific drug class targeted specifically for ME/CFS patients, are there lifestyle changes, preventative massages, or body treatments that you do recommend for people?

Dr. Baraniuk (21:22)**:** Yes. I think an important thing is to realize that your body's playing tricks on you. So you have to marshal your forces, you have to pace yourself, you have to know when too much is too much. You have to plan your day out by saying, "What are the important things that I have to do on each single day?" Can you rest, recuperate, hydrate, be at your best, and then go out and do that function? For example, going to the motor vehicle agency ...

Lisa Horwitz (22:03)**:** We all need to rest before that.

Dr. Baraniuk (22:05)**:** Exactly. Prepare yourself for that stressor, and then come back, come home, and plan to relax. Another situation where that's just very important, just when you have a good day and you feel like you can do anything, and you go out and you try to do everything. And what happens is you rebound, you have the post-exertional malaise, and then boom, you're worse than you were before. You have to limit yourself. Don't try to do too much. This pacing is very, very important.

Dr. Baraniuk (22:48)**:** You can pace yourself another way, which is to look at your heart rate. If you know what your target heart rate is, for example, then you can set a threshold where you would stop exercising, for example, or doing housework if your heart rate reached a certain level. And this may be, for example, 120, 130, 140 beats a minute. It will depend on your age. Staying below that is one way of staying away from the exertional exhaustion.

Dr. Baraniuk (23:40)**:** These types of pacing maneuvers can be difficult to institute by yourself, so it's often useful to get the help of a team. So that could be an occupational therapist to help decide what things you must do and how to find new ways to do them, whether it's for work or even for life by yourself at home. And psychotherapy can also be useful to help with the adjustment that comes from having the severe fatigue. I don't think that cognitive behavioral therapy is going to cure anybody, but if it helps with brain retraining and understanding the limits that you have, then it can be a very good, again, training process to find your limits and help set those limits so that you don't get the exertional exhaustion.

Lisa Horwitz (24:58)**:** And maybe let go of some of the guilt associated with rest. I think we're a very go-go-go world, and there's a lot of — people often look down upon others who have to rest more or who can't go until midnight doing work. They have to sit down. So therapy would be great for that.

Dr. Baraniuk (25:18)**:** This is absolutely true. Absolutely true, and it's one of the reasons that the name chronic fatigue syndrome is disliked so much by patients because it makes it sound as if all they have is fatigue, they're tired, and they're sitting around. They're sitting around because they don't have enough energy to get up and go back to work. If you ask anybody with ME/CFS what they would like to do if they got better, they have a list, they know what they want to do, and they're angry that they can't do those things. That anger, that irritability, the anxiety about, "Am I going to do something that's going to cause me to rebound and get worse in an exacerbation?" Those things have erroneously been called depression, and patients are put on tricyclic drugs or serotonin reuptake inhibitors inappropriately. The key there is people are very angry about this, and CBT [cognitive behavioral therapy] can help with that anger, that irritability. As well, appropriate use of SSRIs can be of value for the anxiety; tricyclic drugs and Flexeril — cyclobenzaprine — can be added in low doses to try to help with sleep, the pain, and some of the cognitive changes.

Lisa Horwitz (26:59)**:** What else would you like people to know who are managing both conditions — ME/CFS and migraine?

Dr. Baraniuk (27:07)**:** Be vocal. Tell people that you have real disease and to cut you some slack. And these are painful diseases. If you explain to people how much pain you get with it, you may be able to get through. Another thing is when you go to see your doctor, don't come in with a shopping list of things you want cured today because you'll get nowhere. When you come in, try to have a list where the worst problems are prioritized, and you start to work on one problem at a time. It can be a slow, frustrating process, but addressing your highest priority issue — whether it's migraine, the fatigue, the cognition — will be better in the long run and will lead to a better doctor-patient relationship.

Lisa Horwitz (28:16)**:** So having manageable expectations about how quickly you can address some of the things you're experiencing?

Dr. Baraniuk (28:23)**:** Yes, yes.

Lisa Horwitz (28:26)**:** Where can we learn more about what you're doing or follow your work?

Dr. Baraniuk (28:30)**:** You can go into PubMed and search for my name, but another good source of information is through the International Association of CFS/ME. It's called the IACFS/ME. They have good patient materials and a very good primer for physicians. The primer you can give to your doctor and help to educate your doctor about the condition. Medical schools are not teaching about these diseases, and the continuing medical education may have to come from the patient.

Lisa Horwitz (29:15)**:** We've learned so much today speaking with you about the overlap of these conditions and just how disabling they can be. I think some of the biggest takeaways I'm taking from this talk is that patients need to be vocal. They need to explore if maybe, if they have chronic systemic pain, if they are also maybe going to be diagnosed with fibromyalgia, because there are treatments to manage that pain. And then, that, in turn can help you also manage any migraine or headache because then you'll be addressing the pain systems at the same time.

Dr. Baraniuk (29:53)**:** So, one of the last things is, the patients can take part in research studies for ME/CFS, for migraine, and other problems like this. Take a look at places like clinicaltrials.gov and see if you are eligible for a clinical trial. There may be treatment studies or other observational studies you can take part in. Very often, it's a wonderful way to learn about your disease and have contact with specialists that otherwise you would have no access to.

Lisa Horwitz (30:32)**:** Dr. James Baraniuk, thank you so much for your time today. I really enjoyed our conversation.

Dr. Baraniuk (30:38)**:** Thank you, Lisa. Much appreciated.