MIGRAINE WORLD SUMMIT®

TRANSCRIPT

INTERVIEWS WITH WORLD-LEADING EXPERTS

NEW DAILY PERSISTENT HEADACHE: PAIN THAT WON'T STOP

ANDREW D. HERSHEY, MD, PhD, FAAN, FAHS
ENDOWED CHAIR & DIRECTOR OF NEUROLOGY
CINCINNATI CHILDREN'S HOSPITAL MEDICAL CENTER
PROFESSOR OF PEDIATRICS & NEUROLOGY
UNIVERSITY OF CINCINNATI COLLEGE OF MEDICINE

Introduction (00:05): Somebody can really look at those four areas — eat, sleep, and exercise, and get adequate fluid hydration — they're well on their way for improvement. You can then introduce additional components, whether it's biosocial components or biopsychosocial components, including the role of cognitive behavioral therapy, which is, how do you cope with pain? So, having coping mechanisms to sort of reduce that anxiety [and/or] depression component of worrying when that headache's going to be bad, worrying when it's going to interfere with my ability to go to work or school or hang out with my friends, do the life-important things that are necessary to do, and having mechanisms to be able to deal with that. So, working on cognitive behavioral therapy. And then the reason I put it, finally, is medication.

Amy Mowbray (00:52): Nearly everyone experiences a headache at some point in their life, but for those of us living with new daily persistent headache (NDPH), we live with headache all day, every day without a break. It is one of the most frustrating and difficult-to-treat primary headache disorders. Dr. Andrew Hershey from Cincinnati Children's Hospital Medical Center is here to help us understand what new daily persistent headache is and how it differs from other headache disorders, such as migraine and chronic tension headache. We're going to look at the different treatment options available and an expert perspective for those struggling to manage new daily persistent headache. Dr. Hershey, welcome to the Migraine World Summit.

Dr. Hershey (01:30): Well, thank you, and thank you for inviting me.

Amy Mowbray (01:32): What is new daily persistent headache?

Dr. Hershey (01:36): So new daily persistent headache has evolved over the last 20 years or so. When it was first recognized, it was the concept where a headache in somebody who's never had headaches before starts and just doesn't go away. So it's new, so it's something that hasn't happened before. It's daily because it happens there every day, hence persistent. So it's continual, 24 hours a day, and just continues. Since that time, and when it was originally described, it was considered a nonmigraine-type headache. So it actually was required to lack migraine features. Over the years, there's been several problems that have arisen from that original criterion. One is the realization that many of the patients with new daily persistent headaches do actually have features consistent with migraine. Secondly is the concept that somebody who has ever had a headache before can't get new daily persistent headaches seemed also to be erroneous.

Dr. Hershey (02:29): So we've broadened the definition a little bit, which has helped further our understanding. So, it's basically a concept, whether you have had headaches or not, you all of a sudden develop a headache that starts and just doesn't go away. Typically, from a clinical perspective, my patients that I see with new daily persistent headaches can tell me — sometimes to the hour, but oftentimes to the day — when the headache starts, and this may have been going on for months or years and just doesn't seem to break. So having an improved understanding of what that is is important to move forward to decide how we're going to treat it and to settle out the differences between the different headache types.

Amy Mowbray (03:10): Who does it typically affect?

Dr. Hershey (03:12): It can start really at any age that it does contribute to. Deciding when it starts and how it starts is probably the next big dilemma that we need to come up with.

Amy Mowbray (03:25): So, we've heard about the persistent head pain. Are there any other symptoms that tend to be present with new daily persistent headache?

Dr. Hershey (03:34): So, it's trying to be teased out. Some of the work that some of my colleagues are working on here in Cincinnati, as well as others, are trying to tease out some of that part of it. They do seem to have a higher degree of disability, although that is also being reevaluated to see, is it truly more disability? The problem is, what's the best comparator to look at? If you compare it to migraine in general, all forms — whether they're infrequent or highly frequent, or nearly every day — those may not be appropriate, especially if they have breaks. But there [are] people who do develop migraine that [have] a migraine consistently every single day.

Dr. Hershey (04:15): Richard Lipton and Steve Silberstein described this process as “transformation”; we now call it “chronification.” But there are a group of people,— and we recognized it 25 years ago, one of our first chronic headache papers in kids — that about a third of the kids we see with chronic headache — so 15 or more pain days per month — have an "always headache," a headache that just doesn't ever seem to break.

Dr. Hershey (04:38): And so, what we're trying to work on is: Can we compare those that slowly transition to the point of having an "always headache" versus those that abruptly start having an "always headache" and to see what differences there are? Historically, we've always thought that the people that have the abrupt onset are harder to treat or take longer to treat. Some recent studies that we've just presented at the American Headache Society meeting this last summer, we've actually shown that the frequency of response — or how well people respond in a survival-curve analysis — was very similar between the continuous headaches and the new daily persistent headaches. And in fact, the new daily persistent headache responded a little bit more quickly than the continuous headache. So that may not necessarily be the right answer for that either. So, some has lots of similarities for those people who have continuous migraines, or who have evolved into continuous migraines and possibly some differences. But further work needs to really sort out those differences. So trying to figure out what triggers off that continuous headache is still a bit up in the air. So, it could be a head trauma; it could be an infection; it could just be a random incident that happens and persists after that point.

Amy Mowbray (06:00): Are there any other triggers that you commonly see other than a viral illness such as Epstein-Barr (EBV) or COVID-19? We've seen the same thing happen in an actual post-traumatic head injury.

Dr. Hershey (06:14): Yeah, I mean post-traumatic and viral — and it does seem to be independent of whatever the virus is — [there've] been some theories about how that could be contributing or a bias factor. If we look at head trauma in particular, one thought is that a significant head injury — and kids, in particular hit their heads all the time, whether it's through sports or tripping or falling or whatever. But not all of them get a persistent headache afterwards. One of the other theories that contributes to this is more on the behavioral/mental health side. Is there a contributor that may be leading to this from anxiety and depression, which we know occurs at a higher rate in people with migraine. It appears that new daily persistent headache patients may have the same degree of influence of anxiety and depression. And could it be that the three factors — whether it's the persistent pain from new daily persistent headache; the anxiety aspect of worrying about, "Are you ever going to get better or what's the cause of this?"; and then the fatalism of aspect of, "Well, I'm never going to get better" — that contributes to the depression. And do these three things cycle together that is

contributing to the anxiety and depression. And once you break that cycle, then everything else can start to get better.

Dr. Hershey (07:32): So, it's a fraction of the 4% of the population that has chronic headaches that has new daily persistent headache. So what makes these people different? And are they really different, or is it just the triggering event that makes them different? And once they've become continuous, they're the same as people with continuous migraine or continuous post-traumatic headache. It does seem to be different than the other primary headache disorders that are continuous, such as hemicrania continual or paroxysmal hemicrania, that are in more in the autonomic or attack-related disorders. So that does seem to be separate. But there does seem to be a lot of commonality between people who have migraine on a daily or continuous basis and new daily persistent headache, which is, should we again be splitters or joiners and what works best for our patients?

Amy Mowbray (08:26): Migraine typically develops and progresses over time, whereas new daily persistent headache seemingly gets switched on overnight. At a physiological level, do we know why this might happen?

Dr. Hershey (08:38): We don't. And that's a good question that really does need to try to be answered: What is that inciting event that just causes it to start?

Amy Mowbray (08:46): Research has shown spikes in the spring and fall months for the initial onset of new daily persistent headache. Why do you think we see these seasonal variations?

Dr. Hershey (08:56): Well, you have to look at what else happens in the spring and the fall months. I mean, depending on where you live, it tends to be storms come through a lot. So we do know, at least in the migraine realm, is that pressure changes from high to low, low to high, is a headache-triggering factor. So could it be just a typical intermittent, infrequent headache is triggered off in the spring and the summer because of that? The other thing that happens in spring and fall is the allergens are higher — and it's not necessarily a cause, and I don't want to say that — but when your body is physiologically stressed by having an allergy, and any of the people who have allergies know you feel more tired, you're more run down. So the allergies themselves may prime you so that a secondary event can trigger something off. And so that also may be a potential contributor. And then also as we transition into the seasons, especially in the fall, is that respiratory viruses and other viruses — whether it's the flu, RSV [respiratory syncytial virus], or even COVID — is rising as people go back to school or more inside. Spring and fall sports are ones that potentially can involve more head contact, whether it's lacrosse or football or soccer or just generally being appropriately active and exercising but can lead to that bump on your head that may set things off.

Amy Mowbray (10:27): Why can those with new daily persistent headache remember so much detail from the day the headache first started?

Dr. Hershey (10:35): Again, I think it may be that anchoring event that something happened. Especially — and this gets into the difference between the slow buildup of headaches. So if we contrast this to somebody who had infrequent headaches and then slightly more frequent and then more and more frequent — that transformation or chronification process — for them, it's not clear when that goes from having a headache five times a week to seven times a week, to it just didn't go away versus somebody that had one or two headaches a month, or no headaches a month, and then all of a sudden had a headache. And so that gives a more clear anchoring

point that that happened. And since that's a dramatic change or a more significant change — especially early on — they're going to remember that and they may record that. They may write it down on a calendar or a diary, or that's the time that they can look at another anchor around that.

Amy Mowbray (11:33): So, how does new daily persistent headache differ from chronic tension headache?

Dr. Hershey (11:38): First of all, chronic tension-type headaches versus chronic migraine in and of itself: Worldwide, there's been a lot more study of chronic migraine, partly because — and this can be a whole topic and discussion in and of itself — is what is the difference between those two entities? Historically, again, the original description of new daily persistent headache more was in alignment with a chronic tension-type headache of continuous type and actually did require that there not be migraine features to make the diagnosis. What evolved, though, was that most people with new daily persistent headache had migraine features, not tension-type headache features. Part of the unwinding of all the echoes is: What is tension-type headache? Is it just a mild form of migraine? Most people are leaning to the fact that once you start to have migraine features, most of your headaches have a migraine aspect to it.

Dr. Hershey (12:40): So, if we look at new daily persistent headache, and that many of them do describe some degree of migraine features, it probably leads more to the migraine phenotype and less of the tension-type headache. Tension-type headaches tend to be nonthrobbing, diffuse in location, not really associated with a lot of other symptoms. And if you ask most new daily persistent headache patients, at some point, either during the day or the week, some of their headaches get to that level of throbbing with light and sound sensitivity. It may not be there all the time. So they've got sort of an "always" component. But then, on the spikes, it spikes with migraine features. So whereas the tension-type headaches — even the chronic tension-type headache and what really hasn't been described well as a continuous form of chronic tension-type headache — they don't tend to have spikes, it's sort of always at a lower-level component. So the spikes may make up the difference between the new daily persistent.

Amy Mowbray (13:33): So, if you have head pain, whether that might present as tension headache, or throbbing, disabling headaches and you have symptoms of migraine associated with it, you're probably more likely to have chronic migraine with daily head pain as opposed to new daily persistent headache.

Dr. Hershey (13:51): No, I think that the new daily persistent also can have those same features. When they have a spike in their headache pain, they oftentimes have the throbbing component to it. The light and the sound may sensitize a little bit more. Now, saying all that, we do know that as people's headaches become more frequent, they may attenuate to some of those associated symptoms. And as they improve, those associated symptoms may become more evident again. Because oftentimes we say, "When your headache's at its worst, what are the symptoms you can relate it to?" And we ask when that happens, both the chronic migraine continuous type and the new daily persistent headache have spikes that have migraine qualities to it. And that's what led to our change a bit in our criteria that say that new daily persistent headache does have migraine features and not necessarily needs to be excluded from that diagnosis if they have migraine features.

Dr. Hershey (14:44): And then that does relate a bit to our understanding of thinking this may be —and I'm speculating here is — its own independent entity, which is what exists in our current

criteria. Or should it be a subcategory of migraine and chronic migraine? And until we have biomarkers that sort that out, we'll probably keep them as independent, but the features continue to overlap. Whereas, if you look at somebody with chronic tension-type headaches, even on their worst days, they don't have migraine features. They don't have features that are consistent with that. So it tends to be that "always lower severity" headache.

Amy Mowbray (15:24): That makes sense. Thank you so much for clarifying that. I know lots of us who have daily headache and symptoms of migraine sometimes can feel a bit lost at what their actual diagnosis is and being given different labels, so that's really helpful. What are the treatment options available for those living with new daily persistent headache?

Dr. Hershey (15:43): Part of it relates to everything we've talked about so far, if we categorize it. First of all, there's been no real isolated controlled studies of just new daily persistent headache. There are a few in the works to try to sort that out, to see if they do have a differential response. One of the biggest challenges for new daily persistent headache, as well as the chronic migraine that are continuous, is essentially all the studies that have been done today exclude that group of patients. Most often, what is now being used for new daily persistent headaches are treatments for migraine, as well as the continuous migraine group. And when we look at that, we do see they do respond over time. Now some of these are nonspecific in terms of treatments. So, one of the things we talk about with all our patients is the importance of healthy habits or just taking good care of yourself.

Dr. Hershey (16:39): Those four areas that seem to be an essential primary focus don't rely on a prescription. It's something people can do without seeing a doctor, but it's really what takes care of your body, takes care of your brain, and may take care of pain disorders. So, adequate hydration — making sure you're hydrating yourself, but using some biomarkers of hydration. Exercise is an important factor, and oftentimes, people in pain, it's hard to exercise. When it hurts, you don't necessarily want to go for even a walk. But it's important to keep yourself mobile, keep yourself active, and work up to an exercise. The third healthy habit is just eating healthy. That means not skipping meals, which can trigger off headaches, but also making healthy food choices. And then finally, the other healthy habit is sleep, which is not just getting adequate sleep in terms of the number of hours, but regular sleep.

Dr. Hershey (17:41): So, having a routine bedtime and wake-up time is important. Many people, especially a lot of adults but also adolescents, are sleep deprived. Typically, and there's good ideas that up to about age 25, you may need up to nine hours of sleep a day. Somebody can really look at those four areas — eat, sleep, and exercise, and get adequate fluid hydration — they're well on their way for improvement. You can then introduce additional components, whether it's biosocial components or biopsychosocial components, including the role of cognitive behavioral therapy, which is, how do you cope with pain? So, having coping mechanisms to sort of reduce that anxiety [and/or] depression component of worrying when that headache's going to be bad, worrying when it's going to interfere with my ability to go to work or school or hang out with my friends, do the life-important things that are necessary to do, and having mechanisms to be able to deal with that. So, working on cognitive behavioral therapy.

Dr. Hershey (18:42): And then the reason I put it, finally, is medication. So, I like to discuss the fact that you can do a lot of things for yourself, and you can do a lot of things that can mentally prepare your brain. But sometimes medications are needed, and without going into specific recommendations, there are spikes in the headaches. And what do you do with one of those

spikes? So having a plan in place, whether it's a medication or a device. And there are many devices out there, but something to do when that headache gets bad while avoiding overuse of it. So you do want to avoid medication overuse. And then [there is] the prevention component.

Dr. Hershey (19:19): So, in addition to cognitive behavioral therapy as a prevention, entertaining some medication prevention that include old things that we've used, which have been more studied because they've just been around longer. So, whether it's the tricyclic antidepressants, or anti-seizure medicines that have been used or some of the newer medications like the monoclonal antibodies or some of the devices, whether it's the condition pain modulation devices — the vasal neurostimulator devices, the TMS devices. So, the good news about that is, you will get better, or we can get you better. It's just that the time factor that does that, and hopefully that does improve.

Dr. Hershey (20:04): Now, one other thing that does contribute to that timing of factors is the earlier recognition of new daily persistent headache or that chronification that's occurred. The earlier interventions that can be entertained — whether it's the healthy lifestyle habits, the acute treatment, and the preventative treatment — the quicker you'll get better. It doesn't say you aren't going to get better; it just may take longer. So, one of the things I really would encourage — and hopefully the audience listening to this — is recognizing that it's a new daily persistent headache and begin that treatment process as early as possible so that patients do get better as quickly as possible.

Amy Mowbray (20:42): It was incredibly refreshing to hear you mention medications last, and different treatments. I know so many of the members of the community and the Migraine World Summit are always looking for other alternatives and not just wanting to hear what medications are available. A recent study in Italy looked into 46 pediatric patients with new daily persistent headache, and 80% of these patients had an initially good clinical response to a migraine prophylactic treatment. But a follow-up one year later, 54 of them returned to a remitting form of headache. Why do treatments become less effective over time, and is this something you see commonly in your own practice?

Dr. Hershey (21:25): So, I think that part of that is, getting better is one thing. Getting to a goal level is even something more so. So, a lot of these studies will look at a 50% response rate. So, if you go from 30 headache days per month — which is what the new daily persistent headache is at — to 15 headache days per month, you've had a 50% response rate. But you're still at a high-frequency headache component. Really, I think a lot of the evidence that we need — you need to get to that one per week. And so, what we've been able to show is, if you can get patients to one per week — and this doesn't necessarily directly [mean] new daily persistent but across the board — that most of the kids will stay that way even after a three- and a five-year follow-up. So, it's not necessarily getting better, but getting better to a goal. And so, as I oftentimes end my visits with my patients, I'll say, “My job here isn't necessarily to treat you but to educate you and so that you can make educated decisions about what you're doing.” And part of my education is to make sure all their questions are answered, and if I can't answer a question, that's why we do research.

Amy Mowbray (22:36): What advice would you give to someone who feels like they have tried everything? They're doing the lifestyle stuff; they are taking medication, but they are still experiencing unrelenting daily headaches.

Dr. Hershey (22:48): I mean, I think one of the biggest things is to look at the team you have to help take care of you. It may be helpful to expand that team. As physicians, we should never be upset or apologetic about getting a second opinion or referring somebody. They may have new ideas. It's always better to get new ideas and not get locked in to something, whether it's the patient themselves or the physicians taking care of themselves. On the other hand, if there's no new ideas, it's oftentimes reassuring to say, "You're on the right track. You just need to give it more time. You need to incorporate these things." Or finally, if you're one of those patients who has tried everything, and you are on the right track, and it's still not getting better, is look to volunteer for a research study.

Amy Mowbray (23:36): Lastly, do you have any success stories you could share of patients who have gotten better from new daily persistent headache?

Dr. Hershey (23:43): There's one I oftentimes like to tell — a couple of different ones, kids-related. But one was a boy that came to me in his sophomore year in high school. So he was in 10th grade. He really liked football, which as a neurologist, I can't really necessarily recommend you banging your head against somebody else, but I tell this story. But one of his complaints when he developed his headache — and it wasn't a post-traumatic and triggering event. He had just, over the summer, had developed a headache, potentially was dehydration, but we really don't know the cause. But his biggest complaint was that just going out and throwing the football for five minutes with his dad worsened his headache. And so we talked about, we're going to work with you. But he was very motivated with the exercise component because it was something that he really valued. It took him a year and a half to get to the point that he was back in exercising. But by his senior year in high school, so his 12th grade year, he was back on the football team and actually got a college scholarship for playing football. So it really, again, it took time, but he was motivated to do that because that was something that he really, really was involved with. I saw him many years later. He still was having intermittent headaches, but he was well controlled and very thankful for that.

Amy Mowbray (25:06): Where can we learn more about what you're doing or follow your work?

Dr. Hershey (25:11): So, there's a variety of resources. I mean, for us in particular, we're at Cincinnati Children's. You can just look in the Headache Center. We do list some more active research that's going on. You can go to clinicaltrials.gov, where all the clinical trials [are] and search for “headache,” search for “new daily persistent headache.” The NIH itself (National Institutes of Health), has multiple resources for pain disorders, including a patient's advocacy arm that's contributed there. And then, as well as our medical societies, including the American Headache Society and the International Headache Society, have a lot of resources for patients who can put you in contact.

Amy Mowbray (25:48): Dr. Hershey, this has been a fascinating insight into new daily persistent headache. On behalf of those living with unrelenting headaches, thank you for taking the time to share your expertise with us today at the Migraine World Summit. Thank you.

Dr. Hershey (26:02): Thank you for inviting me.