Vanderbilt Audiology Journal Club: Relationships Among Vestibular Disorders

Recorded: Dec 11, 2019

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AudiologyOnline.com Course #34161

- [Christy] At this time, it is my pleasure to introduce our first presenter, who will kick off this year's journal club and also introduce the remaining two presenters. Dr. Gary Jacobson is the professor in the Department of Hearing and Speech Sciences at Vanderbilt University and the director of the division of audiology for the Vanderbilt Bill Wilkerson Center for Otolaryngology and Communication Sciences. Welcome back, Dr. Jacobson. We look forward to hearing from you and the team. And at this time, I'll hand the mic over to you.

- [Gary] Thank you very much, and I wanna welcome everyone. Welcome to the Vanderbilt Audiology Journal Club. We hope you're all safe and warm. And we hope to give you some things to think about over this next hour. I'd like to introduce my co-presenters. The first is Dr. Kelsey Hatton. Among her many functions, she functions as our vestibular science study coordinator. I'd also like to introduce Dr. Richard Roberts, who is vice chairman for clinical operations in the Department of Hearing and Speech Sciences. And that includes not just audiology and vestibular sciences, but also includes speech pathology and OT and PT. I think it's a pretty common experience to evaluate a patient, and in the end, have evidence of two or more underlying conditions that could explain the patient's symptoms. The underlying theme of today's presentation is that it is, indeed, possible for a patient to have two or more co-existing, underlying dizziness disorders that explain the patient's presenting symptoms. So the general theme of our presentation today is going to be recognizing the presence of multiple coexisting dizziness diagnoses. These are the primary references for our presentation this morning. The first paper that will be reviewed by Dr. Kelsey Hatton is an older paper. So this is sort of something old, something new. This paper was published in 2005 and was authored by Dr. Joseph Furman and his colleagues at the University of Pittsburgh. And the title is "Migraine-anxiety related dizziness: "a new disorder?" The second paper is titled "The interrelations "between the different causes of dizziness: "A conceptual framework "for understanding vestibular disorders." And this was a multinational effort. This paper appeared in "Annals of Otology, Rhinology &

Laryngology" this year, and I will be reviewing that paper. To be comprehensive, I've added one final reference that will not be reviewed. However, it's worth reading. And the title of that article is, appropriately, "The Dizzy Patient: Consider a Second Diagnosis." That study was published in 2017, and the paper was authored by van Leeuwen and colleagues. We'll end this year's journal club with some data from a recent study conducted by Dr. Richard Roberts that is pertinent to this topic. And he will be presenting the data. We're going to find out that, not infrequently, a patient may have multiple coexisting diagnoses. And the recognition of this finding may enable healthcare providers to be more effective in their diagnostic and treatment efforts. These are our learning outcomes for today. And with this as a brief introduction, the briefest of introductions, I'm going to hand off the microphone to Dr. Kelsey Hatton, who will discuss the first article.

- [Kelsey] All right. So I'm gonna start with our migraine-anxiety related dizziness disorder. So first, I wanted to just establish some baseline definitions before we get into talking about these disorders occurring in the same patients, and also kind of when they co-occur and the issues that come up with these patients. So with migraine, we know that the headaches are characterized by, typically they're unilateral or focal. And they're characterized by having other neurological symptoms, sensorimotor, language changes, or brain stem changes. But the typical thing is that these changes are temporary and fully reversible once the patient passes the period with migraine. With anxiety disorders that are at a clinical level, patients would have excessive fear or anxiety, but it would lead to a behavioral disturbance. So they have problems with social functions, occupational functions, maybe activities of daily living, self-care functions. So their anxiety is at a level that is more of a tipping point into interfering with their life functions. And then with dizziness, it's a disturbance or impaired spacial orientation without a false sense of distorted, false or distorted sense of motion. We know that vertigo is more of that actual sense of motion. And dizziness, when we talk in the general sense, not in the definition provided by the international classification of vestibular disorders here, we're thinking that extends into unsteadiness, postural

disturbances, visual-vestibular reported type symptoms. So these three problems, they often have secondary health conditions and require lots of specialty care to get adequate management. So the specialists that work on these disorders are really in disparate fields. And even though we have, in the American healthcare system, the primary care doctor as the home of care, the base of care, the specialists that are working on these areas for these patients will have to communicate information about their care to the primary care doctor or to one another before they may really realize that there are separate disorders that they are not necessarily managing that could be part of a overall pattern. And we have to take a more holistic approach for these patients to have this kind of multi-disorder diagnosis recognized. So it's kind of hard to have a provider that's a neurologist that really feels comfortable working on anxiety and dizziness disorders and thinking about it as a total picture. So really, to write a diagnosis like migraine-anxiety related dizziness, you would need the provider that's giving the diagnosis to be aware of each individual disorder occurring in that same patient. They would need to know that there's a possibility of these particular disorders interacting, and then recognize that these three disparate disorders could be controlled by a single or a shared physiologic function. So it's a little tricky because of the way our healthcare system is set up and how we're very highly specialized in getting these patients a more overarching, holistic care, team approach.

So I wanted to break down some of the prevalence and impact factors for each of these disorders, because we're not always familiar with the incidence of these things occurring in our population. So migraine is very common and can occur in children as young as 18 months. And it occurs often, for part of people's lives, it'll be really bad in adolescence, but it'll be better in adulthood. Or it'll come back after a pregnancy or be more prevalent in elder adulthood. So it can change across a lifetime. And the way that it presents is variable from person to person. But one in four households include someone with migraines in the United States, and 90% of sufferers have a family history of migraine. So your patients are typically going to say, oh, yes, I have a sibling, a cousin, a parent, a child, who also suffers from these problems. Even if they haven't

had formal diagnosis, that's something that happens a lot with our patients in clinic. And it's a very disabling problem that has a high financial impact on these families. So it's estimated that a family with someone who has migraines is spending 70% more on their healthcare costs annually than other families. And they're losing more work time. So not only are they losing money that they're paying towards health care, but they're also losing time to be able to pay for that health care. Because they aren't able to function when they're having these neurological effects and headaches that really prevent them from being in a normal daily activity kind of setting. So it's also estimated that these patients are really often undertreated or that they aren't seeking treatment, even when they fall into a pretty severe category of having migraines. So we know it's common, it's disabling, and it's often undermanaged. There's a lot of research about migraine. It's still a very uncertain, you know, there's not one cause that they've really pinpointed for migraine.

So these are the three most common suggested causes of migraine, the ones that have a lot of research behind them. And the first two are really the ones that people think are the ones occurring for vestibular migrainers. But the thing to note is that there is these complicated pathways with multiple centers of processing occurring, and what they really require to function correctly are monoaminergic neurotransmitters, meaning they are neurotransmitters that have one amino group in them. So this is serotonin, dopamine, epinephrine, all the names that you know from your biology classes about neurotransmitters, so the chemicals that are helping us relay those neural signals and create neural signal transmission through the body. So the thing to note about this little simplified diagram is even if someone is having dysfunction in the trigeminovascular reflex pathway, they could have concurrent dysfunction in the thalamic and cortical processing. So again, we're talking again about things that may be happening concurrently or in parallel, so the picture is pretty complicated when it comes to trying to figure out what exactly is causing migraines. When it comes to anxiety, we have, again, a large proportion of the population that are affected by anxiety disorders at some point during their life, about 1/3 of people. And again, this is something where, if

there's someone else in your family who has this issue, you are more likely to have this issue than if you had no one else in your family with an anxiety disorder. And these are the most common medical, mental diseases. And they're under-recognized, undertreated. And there's a lot of stigma associated with them still. So that's part of why it's estimated that we are not taking care of these patients very well. Because they are not necessarily willing to undergo treatment for social reasons. And again, this is something that costs patients more if they are having this particular problem, especially if they are a patient with migraine. So patients with migraine and anxiety, on top of spending more in their family, compared to people without migraines in their family, they are spending $4,500 more per year in healthcare costs because of this anxiety component of things that is often co-occurring. So it's common. It's impactful. So when we talk about what is causing anxiety on a kind of brain, neurochemical level, there's a circuit in our brain that's really connecting the way that we process our emotions and sensory input. And this system really depends, again, on neurotransmitters that have one amino acid in them, or one amino acid group.

And so what I'm illustrating here is that, like we talked about with migraine, that you can have more than one pathway occurring with this circuit. You could have only one kind of circuit being reinforced by the person's neurotransmitter dysfunction, or you could multiple circuits occurring simultaneously and in parallel to cause these vertigo and postural instability symptoms secondary to anxiety. But the problem with anxiety disorders and why they're so challenging to manage is that we're creating that feedback loop that's getting strengthened while we're being vigilant. So higher anxiety and stress leads to higher vigilance. And then they are reinforcing this pathway neurochemically and prolonging the symptoms and the activation of the threat circuit. All right, so hopping over to dizziness, we know dizziness across the lifetime is relatively common and that BPPV, vestibular neuritis, Meniere's disease, and vestibular migraine are thought to be the responsible disorders when we talk about the bulk of dizziness coming from the vestibular system, or from the brain. But the pathophysiology differs by the different balance disorders. And usually, historically,

we've been thinking of these things from an ear-based perspective. So usually, it's a physical problem in the ear that leads to changes, to neurotransmission, and that's more of the secondary effect of the vestibular or balance disorder. Now, so we've kind of gone over all of those. And across the lifetime, each of those disorders is pretty common. If we look at the population right now, and they talk about prevalence, that with migraine, about 14% of the general population right now is having migraine, and then about 7% have vertigo. And if you said seven plus 14%, you know, we should be getting 21% of people that are affected by either of these things and maybe a small proportion of that 21% has both of those things. But really, the math doesn't quite add up like that. It's really more recombinant, where we would expect, from statistics, that if these disorders were randomly co-occurring, it would be 1%. Really, it's three times as high as that.

So again, the shared pathway argument, that there's something in common with these things, is very, we are very kind of influenced by that. And we would think, yes, that makes sense. When it comes to migraine and anxiety, again, a high proportion of patients that have migraine are thought to also have comorbid anxiety disorder. And if we look at it from the side of saying, generalized anxiety disorder is the highest proportion of patients with anxiety disorders that are diagnosed, they are 3.86 times more likely to also have migraine. So again, a shared higher incidence of both of those things occurring together than what we might typically suspect would happen. And then with dizziness/anxiety, if you don't have balance disorders but you have anxiety, that distribution of the population is totally separate. There's no overlap on the Venn diagram of people with dizziness and anxiety and people with anxiety without dizziness or balance disorders. So again, there's something about the fact that these things co-occur. So the overlapping etiology, you know, the point that I was emphasizing with each of those disorders and the etiology behind them is really, we think that there is dysfunction in how neurotransmitters are used for these patients. So for anxiety and migraine, it's serotonin primarily used in some of these pathways. Dizziness and anxiety, again, it's serotonin and epinephrine as the primary neurotransmitters used in

a particular area for processing this information. Dizziness and migraine, again, serotonin is highly active in the trigeminal pathway. So the proposed combination from this paper is that all three disorders have an underlying neural circuitry that's shared and requires appropriate use of, especially, serotonin in order to process information appropriately. So what do you expect from these patients on a clinical level? Well, in clinic, when they come in, they really will present in a very variable fashion. And what's bothering them the most might be different from person to person. But what is very interesting is people that come in to dizziness clinics, or at least in our experience here, a lot of those patients that have migraine and anxiety will have a strong visual preference. And so they really depend on their eyes for their cues for balance. They do not like being put in the dark for your evaluation. And when you take away their visual cues, they're very disoriented very easily.

So these are the people that you're coaching, you know, that we need to have our hands on sides, holding the chair, pressing their legs down into the chair, trying to give them some kind of somatic input, because they just, you close up the goggles, and they don't have any clue where they are anymore. So this visual dependence and disorientation when they don't have their vision is very strongly driven by visual motion as well. So you can just put a pattern on the wall, or if there's a pattern on the carpet, these are patients that will definitely notice very busy patterns. They will comment on them to you without any prior discussion. I have had patients come in that have migraine and dizziness, and likely anxiety through the course of the appointment when we were talking with them, and they said they're sitting at an intersection, and someone else pulls out in front of them with their car, maybe making a left turn through a four-way intersection, and they have to stop and kind of catch themselves for a minute, because they can feel that they're gonna go into a spell just by watching a car move across their visual field. So these are people that, they go into a store shopping for something, and they have to leave because they are just overwhelmed, and they wanna prevent themselves from going into a spiral kind of situation. So what do we do to treat these patients? Because they are going to have multiple things going on. And

you know, it's not all within our scope of practice. So really, we need to participate as a team player and work with our physicians and the patient's primary care doctor to explain kind of what's going on and why they might be having more than one element to their problems. And what's really effective for each of these different disorders is vestibular rehab therapy. So because they're really working on the symptoms, and the therapy is driven by the symptoms the patient is reporting, this therapy tends to be helpful for all patients. And they do include visual-vestibular integration exercises for a lot of patients that undergo VRT. And that seems to be very helpful in reducing the person's weighting on visual preference, and maybe help them organize things so they're paying better attention to the vestibular signals, to the somatosensory signals for maintaining their balance.

Now, in this paper, because it was written by a group of physicians, they also talked about classes of medications. Now, this is nothing that an audiologist is going to prescribe, but it's something that might be helpful if you have a patient that you suspect has migraine and anxiety-related dizziness that you would talk with your managing physician or group physician and say, you know, this is a paper about this, and maybe these are things that haven't been tried or might be helpful to discuss for this patient. So beta-blockers were noted to be unhelpful, but various other classes were helpful depending on what the patient's primary complaints were. So overall, we know that when we talk about migraine, anxiety, and dizziness and balance disorders, that these are co-occurring at a higher rate than any one disorder alone. And there's a common pathophysiology suspected for all three conditions that is neurotransmitter-driven dysfunction. And our role is to really try to be part of, make sure to encourage the patient to advocate for themselves within their medical care team and discuss these other things that maybe they aren't talking about with their primary care doctor. Or maybe they haven't recognized that they are having migraines or that they are having anxiety that's at a clinical level. So just encouraging them to really open up the discussion about those problems with their medical team. And then also, encouraging the physicians that VRT can be helpful for all of these disorders and should help

patients with multiples of these disorders. And I always include too many references, but there's lots of great reading on here. And if you need any of these classification systems to share with your colleagues, with your students, with your care teammates, there's always good things at the bottom from the Migraine Research Foundation, the International Classification of Headache Disorders, the DSM, and the International Classification of Vestibular Disorders. So I'm gonna hand off the baton back off to Dr. Jacobson to talk more about the paper by Zhu et al.

- [Gary] Thank you, Kelsey. This is the paper I'm reviewing, "The interrelations between different causes of dizziness: "A conceptual framework "for understanding vestibular disorders." It's a big, long title. By way of background, dizziness, of course, is a very common symptom. The authors report a one-year prevalence of almost 15% in adults. And further, the authors state that most patients receive a single diagnosis. However, almost 4% receive two or more diagnoses. Additionally, it probably is no surprise that the most common dizziness diagnosis is BPPV, followed by vestibular neuritis, Meniere's disease, and vestibular migraine. In aggregate, these diagnoses account for between 33 and 70% of all dizziness diagnoses. However, patients may present to the clinic with symptoms that don't fit a single diagnosis. The present report represented an effort to coalesce the existing literature and determine whether there was evidence supporting the contention that it is common for patients to have multiple coexisting sources that contribute to the symptom complex. In the author's words, and I quote, "We hope to move away from an exclusionary approach, "where one diagnostic entity "is held responsible for the symptoms, "to a more inclusive approach, "whereby multiple diagnoses are entertained and treated." The purpose of this literature review, and this is the one that the authors are presenting, was to summarize the relationships in this interconnected web of diagnostic entities. This study represented a review of the literature on the topic of multiple coexisting dizziness diagnoses. The data source was PubMed. The studies were prospective and retrospective and observational, incorporating questionnaires, surveys, telephone interviews, chart reviews, and database analyses. The search terms they used included dizziness, vertigo,

epidemiology, cause, differential diagnosis, cohort, diagnosis, and multiple diagnosis. And the articles were included in the review if they described the epidemiology of co-occurrences and overlapping symptoms of different vestibular disorders. The authors reported their results using descriptive statistics. This list shows the diseases and disorders that were considered in the article. And I'll be addressing, actually, most of these, albeit briefly sometimes. This slide shows what percent of the total number of patients in the review had single diagnoses. And it can be observed that for roughly 41% for the patients, a single diagnosis could explain their symptoms. This slide shows some of the more commonly described pairs of co-occurring diagnoses. These included the pairing of vestibular migraine and Meniere's disease, the pairing of vestibular migraine and BPPV, the pairing of vestibular neuritis and BPPV, and the pairing of persistent postural perceptual dizziness and all of the other diagnoses.

Without getting too far ahead of myself, I'd add here that we have found in some individuals as many as three to four coexisting dizziness disorders. This is a table that summarizes the data presented in the review. Notice, for example, how many diseases and disorders have been found to co-occur with BPPV or vestibular migraine. So let's take a look in a little greater detail at some of these co-occurrences. The first co-occurrence is between vestibular migraine and Meniere's disease. We know that vestibular migraine has a lifetime prevalence of approximately 1%. The prevalence of Meniere's disease is somewhere between .2 and .5%. Although the mechanisms that are common to the diseases are unknown, the interconnections have been well-reported. For example, the authors report that 81% of patients with Meniere's disease reported a history of migraine. That value was closer to 33% for normals. Also, the lifetime prevalence of migraine is 56% for patients with Meniere's disease compared to 25% of those without Meniere's disease. In another report, 95% of patients with vestibular migraine reported at least one migrainous symptom, which included migraine aura or photo- or phonophobia. How about the co-occurrence between vestibular neuritis and positional vertigo? The authors reported that vestibular neuritis is the second most common vestibular disease, occurring 3.5 per 100,000 persons.

And further, 5.2% of patients who demonstrated positional vertigo and vestibular neuritis were younger, were more difficult to treat, and required a larger number of therapy sessions to show improvement compared to patients with idiopathic BPPV. How about the co-occurrence of vestibular migraine and positional vertigo? Since diseases affecting the vestibular end organ may affect the otolith membrane, within which the otoliths reside. It's not surprising that these diseases might result in the migration of otoliths from the utricle into the semicircular canal system. The effect would be an initial, longer-lasting, severe vertigo that would be followed later by shorter and intense spells of vertigo lasting seconds. It has been reported that BPPV occurs between 38 and 55% of the time for patients with vestibular migraine. And the authors reported a study of 500 patients evaluated in a balance clinic. And 1/3 had migraine, and 42% of that subgroup had BPPV. How about the pairing of Meniere's disease and BPPV?

This is another instance whereby a primary vestibular disease could evolve into a more chronic, secondary positional vertigo. We know that BPPV occurs with Meniere's disease between 3.7 and 8.4% of the time. This occurs more often for women than men. And also, the authors reported that BPPV affects the horizontal canal more often. And it's been reported to be more difficult to clear using appropriate repositioning maneuvers. The co-occurrence of vestibular migraine and bilateral peripheral vestibular system impairment has been reported. Bilateral impairment has a prevalence of 28 per 100,000 persons. In one study referenced by the authors, 50% of patients with idiopathic bilateral peripheral vestibular impairment had migraine compared to 11% of patients without idiopathic bilateral peripheral vestibular impairment. How about migraine and superior canal dehiscence? The authors have reported a prevalence of superior semicircular canal dehiscence of between .5 and 1.4%. Interestingly, there has been a reported relationship between vestibular migraine and superior semicircular canal dehiscence syndrome. More specifically, it's been reported that SCD with vestibular migraine occurs 47% of the time for women. And of note, 25% of patients with SCD and migraine have reported improvement in migraine after the surgical repair

of the SCD. This slide shows some of the connections the authors report between PPPD, vestibular migraine, Meniere's disease, and BPPV. Anxiety is a common accompaniment to dizziness. In fact, chronic subjective dizziness, which was a precursor to the contemporary term persistent postural perceptual dizziness, or PPPD, was a type of dizziness that occurred often in conjunction with anxiety. Patients with CSD often had an antecedent history of vestibular impairment or anxiety disorder. Those were unimpaired and who then suffered an ear disorder and became anxious were diagnosed with otogenic CSD. Those whose primary disorder was anxiety, and it was the anxiety that was the source of the dizziness, were diagnosed with psychogenic CSD. And those with premorbid anxiety who suffered an ear event and then became chronically dizzy were diagnosed with interactive CSD. Given these definitions, it's easy to imagine how one type of dizziness could evolve into another. This slide provides an example of a common sequence of events that would result in a patient experiencing three different dizziness disorders.

This patient is a 62-year-old male with an initial episode of true vertigo lasting several days. After two weeks, he was improving to a point where he was close to baseline. However, as his vertigo disappeared, he became aware that he was experiencing brief spells of intense vertigo that were triggered by head movements. He received a particle repositioning maneuver, which improved his motion-provoked symptoms but left him with continuous dizziness that he described as a constant rocking sensation that at times progressed to panic attacks. In this example, the first example was undoubtedly true vertigo and most likely represented a vestibular neuritis. The neuritis then evolved into an ipsilesional BPPV due to the weakening of the otolith membrane and migration of the liberated otoliths into the semicircular canals. The BPPV then transitioned into an anxiety-related dizziness which was most likely PPPD. To conclude, in the same manner that BPPV is a secondary diagnosis, can originate from the primary diagnoses of vestibular neuritis, Meniere's disease, or vestibular migraine, it is possible for the primary diagnoses of BPPV, vestibular neuritis, Meniere's disease, and vestibular migraine to evolve into a PPPD. The authors state that they now conceptualize

vestibular disorders as a series of overlapping symptoms and multiple dizziness diagnoses in the same way we know that there are multiple overlapping contributors to falls in the elderly. In their review, the investigators reported that the largest number of overlapping diagnoses involved migraine and vestibular migraine that may co-occur with BPPV, Meniere's disease, superior canal dehiscence, and head trauma. All right, that takes us the my colleague, Dr. Richard Roberts, who will now give you a peek at some very interesting related work that he has completed in this area.

- [Richard] Thanks, Gary. I think it would be good if we first summarize to this point. Dr. Hatton has shown, through the work of Furman et al., there's physiologic support for the overlap of migraine, anxiety, and dizziness. Dr. Jacobson, through the paper by Zhu et al., has shown there are interrelations among various vestibular disorders, and even non-vestibular disorders like anxiety, aging, head trauma, et cetera. Both of those points reinforce the importance that clinicians should consider the possibility of interrelations during assessment and management of patients with dizziness. If we look back at the paper by Zhu et al., there are a few important considerations. Those authors analyzed 18 published epidemiologic studies. One study was completed by telephone interview with patients, and one used a patient questionnaire to determine differential diagnosis. The remaining almost 90% of the data that they considered used diagnosis data or differential diagnosis that was developed from the perspective of the physician. So there work truly, overall, represents the point of view of the physician. The second consideration is Zhu et al. determined 3.7% of the patients had multiple diagnoses, not just a single diagnosis. So based on their analysis of the data, that means 96.3% of patients only have one diagnosis. If that's true, then why is it important to consider this? Why do we have three papers today that we're talking about that relate to this? The fact is that the individual patient that's within that 3.7% doesn't care at all that there are not many people falling into that group. They only know that they feel terrible and they wanna feel better. The second consideration related to that is that there are other studies that report multiple diagnosis data, and some of those identify a much larger percentage, up 35% of patients having multiple

diagnosis. A final consideration that other studies have described is that there are often relations between a couple of vestibular disorders, like BPPV and migraine, for example, or Meniere's disease and migraine. This investigation that Dr. Jacobson discussed by Zhu et al. is really important because it represents an attempt to describe the interrelations across multiple disorders, not just two. And really, other papers have not done this before. So this is an important study. We wanted to explore these relationships further, and we were fortunate to have kind of a unique opportunity. Last year, Dr. Jacobson described the results of the dizziness symptom profile. Recall, this is a 31-item self-report questionnaire developed to help create a differential diagnosis. A differential diagnosis, you will also remember, is a list of possible disorders that may explain a set of symptoms.

So we have a data set collected from the perspective of the patient, which differs from most of the investigations reported by Zhu et al. The data set was collected to develop differential diagnosis, which is exactly what Zhu et al. were interested in researching. And the data were collected for a different purpose than the purpose of the current investigation. That means the opportunity for investigator bias in the current reanalysis of the DSP data is reduced. Our primary purpose of the current investigation was to determine if interrelations between vestibular disorders reported by Zhu et al. using data generated from the physician perspective would be supported in a data set generated from the patient perspective. As a review, the 31 items of the DSP converge on seven factors. That's supported by the statistical analysis described in Jacobson et al. Those factors overlap directly with six vestibular disorders in a more generic area, unspecified or unsteadiness. The paper published last year described three investigations that encompassed development of the DSP. The purpose of Investigation 3 in that series was to compare the differential diagnosis generated by the patient using the DSP to the differential diagnosis of the gold standard developed by ear specialists. Overall, the DSP converged on a differential created by the ear specialist 70.3% of the time. That's consistent with two other investigations that have attempted to develop a similar self-report measure. In that particular project, 195

subjects were recruited from patients seen at our center for evaluation of vestibular dysfunction. Mean age was almost 60, and the majority of the subjects were female. Those demographics are what you would expect in a practice with a focus on dizziness. Remember, in the DSP study, we compared the DSP data, which was patient-created, to the physician data. In the current investigation, we did not include the physician data at all. We only considered the patient-generated DSP data. It's also important to keep in mind that because of the way the data were developed, there was no restriction on number of diagnoses endorsed by the patient. On the left, it's a little blurry, but you can see a sample of DSP items like, "I get dizzy when I turn over in bed." the patient indicates their low level of agreement with each of the 31 statements using a four-point Likert scale, ranging from strongly disagree to strongly agree. The results from all 31 items are then used to create the differential diagnosis, an example of which you see on the right. In this example, the patient would have a differential diagnosis that included vestibular migraine and BPPV.

So this was completed for those 195 subjects for the DSP study. For this investigation, we simply took the 195 data points and reanalyzed them. The first thing we wanted to do was determine the frequency of diagnoses by patient, or the sample. The majority of the 195 patients, 133 of them, almost 70%, only had a single diagnosis. About 30% endorsed two or more. It was uncommon for a subject to endorse four. And no endorsed more than four using the DSP. If we compare this result with Zhu et al., we're much higher. Remember, Zhu et al. reported 3.7% of patients had multiple diagnoses. Now, not every study they used even reported multiple diagnosis data. But Zhu et al. did include all of those participants. If you recalculate their percentage of multiple diagnosis patients using only the studies that included multiple diagnoses, they're closer to 14%, which is still lower than our data, but it falls within the range of other published data for multiple diagnoses. If we compare our data with the other published data, up to 35% of patients had multiple diagnoses in some investigations. Our data fall within the reported range and are in close agreement with two specific studies, one by Uneri and Polat, who found 35.1% of their patients had multiple diagnoses, and van

Leeuwen, that Dr. Jacobson mentioned earlier, 30.1% of their subjects had multiple diagnoses. So there's really a lot of evidence that suggests around 30% of patients may have multiple diagnoses. That close agreement helps support the validity of our data set. The next step was to take a closer look at the data of the 68.2% of patients that endorsed only one disorder. The categories Other, BPPV, and Vestibular Migraine accounted for 80.4% of the diagnoses in the single-diagnosis data. So those were certainly the most common. We chose to eliminate Unsteadiness, which you see here, that accounted for 10% of the diagnosis data, from further consideration, because so many non-vestibular factors can influence that. The category Other was actually the most common. But BPPV and Vestibular Migraine were also very common, which is typical in many epidemiologic studies of diagnosis data. Persistent postural perceptual dizziness, PPPD, was the least common single diagnosis, which was not surprising, since most patients with PPPD have prior or coexisting vestibular disorder that leads to the PPPD. We did wanna look a little further at this seemingly vague Other category.

Many epidemiologic studies report similar nonspecific categories. This often accounts for between 11 and 21% of diagnoses. And that's lower than we observed, our almost 40% in our data. The point here, I think, is this large percentage of patients grouping on this nonspecific category underscores the challenge that healthcare providers experience with assessment and management of patients with dizziness and imbalance. Clearly, it's a challenge to place some patients into a vestibular disorder category. Quite simply, there may not even be a vestibular disorder causing the symptoms. This figure shows how our single-diagnosis data compare to Zhu et al. as well as other investigations. The diamonds represent the percentage of patients in the current study by diagnosis. The squares represent the Zhu et al. data. Ranges are provided from other published investigations by disorder. Our data are very close to Zhu et al. for Meniere's disease that you see here, PPPD, and superior canal dehiscence. We're within the range of other reports for BPPV and vestibular neuritis. We did observe a larger percentage of patients with vestibular migraine than Zhu et al. but were within 1% of another published study by Muelleman et al. that you see right

here. Together, these results indicate that DSP data provide a valid representation of vestibular diagnoses, even though the data were generated by patients and not physicians. Because of this, we should be able to support the assumption that the multiple diagnosis data is also valid. That moves us to the next phase of the current study. We wanted to look closer at the multiple diagnosis data. 62 subjects, so 32%, of the sample had two or more diagnoses. We see similar trends as we observed in the single-diagnosis data. BPPV and especially vestibular migraine are far and away the most common diagnosis in this group. The rates of occurrence are much higher for both disorders compared to other vestibular disorders. Vestibular neuritis is third most common at almost 40%, 37%. And the remaining are all somewhat similar, ranging from 21% to 27.4%. As expected, we do see PPPD go from a rate of .8% in the single-diagnosis data to 27.4% in the multiple diagnosis group. That's consistent, again, with expectations as described by Dr. Jeffrey Staab. It was more challenging to identify studies that separated out their subjects with multiple diagnoses from single diagnosis for comparison to our data. These four investigations did allow for some comparison. No other investigations were identified that reported on PPPD and SCD in patients with multiple diagnoses.

So you only see our data there. Our data for BPPV, Meniere's disease, and vestibular neuritis fall within the other data ranges reported for patients with multiple diagnoses, though we were usually towards the higher end of the range. We were almost 20% higher, if you look here, so right at 80% of our patients had vestibular migraine. So 20% higher than the next highest percentage. So that does bring up the question, is our data for vestibular migraine correct or incorrect? It seems less likely that this is an incorrect or false finding. We do have some level of confidence within identification of vestibular migraine using the DSP. Because in Jacobson et al., we observed 95.3% agreement between DSP results and the gold standard ear specialist diagnosis for vestibular migraine. So if the DSP indicates vestibular migraine, it's correct, compared to that gold standard, 93% of the time. Also, our data for single diagnosis are within 1% of the other published data, supporting validity of the DSP. It should be the case

that our data for multiple diagnoses are also valid. We may have just had more migrainers or DSP is more sensitive for vestibular migraine than the methods of the other studies. Next, we wanted evaluate the percentage of co-occurring diagnoses in comparison to the data reported by Zhu et al. This table is an adaptation of their data, kind of like the one that you saw for Dr. Jacobson. Our data extends that reported by Zhu et al. to additional core and co-occurring diagnosis percentages for six vestibular disorders. The extended data are highlighted in this table. There's agreement between the rates reported by Zhu et al. and the DSP for the core diagnosis of Meniere's disease and rate of co-occurring BPPV, as well as co-occurring vestibular migraine. You do see there's high variability across studies used to create the ranges in Zhu et al. And that could have made it easier to find agreement for these co-occurring diagnoses. We found fewer subjects with a core diagnosis of vestibular migraine and co-occurring diagnosis of Meniere's disease. Zhu et al. reported a range from 25 to 38%. We identified 16.3% of patients with vestibular migraine also having co-occurring diagnoses of Meniere's disease.

Still that's reasonably close to the lower limit of what's been reported for that group. It's within 10%. Most often, though, we identified a higher percentage of co-occurring vestibular diagnoses, as you see highlighted here. It's possible this relates to the fact that we placed no limit on number of diagnoses. That could increase the chance of identifying co-occurring disorders. As you would expect from the distributions observed in the single-diagnosis and multiple-diagnoses data, we swallow the highest percentage of co-occurrence for vestibular migraine, which ranged from 47.1 to 87.5%, and BPPV, which ranged from 41.2 to 56.3%. These two appear to be not only common disorders but also common co-occurring disorders. A striking finding that I'll point to here is that 87.5% of our subjects with superior canal dehiscence also had vestibular migraines, almost 90%. That's in agreement with what we hear from our neurotology colleagues, who will often treat vestibular migraine in that group prior to surgical intervention. A final step in our analysis was to consider the common patterns observed in the multiple diagnosis group. BPPV plus vestibular migraine accounted for

4.6% of all the subjects, you can see, which is pretty high. You can see that out of the overall group of subjects, the other patterns with more diagnoses were not as common. Still it's interesting that BPPV and especially vestibular migraine occur in most of these multiple patterns. In fact, as the number of diagnoses increases, the percentages that vestibular migraine and BPPV occur also increases. Vestibular migraine is definitely the most common disorder when multiple diagnosis is considered together, and also for the three- and four-diagnosis groups. So by the time we looked at the patterns when people had four diagnoses, every one of those patients had vestibular migraine as a co-occurring issue. That brings up the question whether vestibular migraine is special in terms of being the most common interrelated disorder. Zhu et al. certainly felt that way. They advocated screening for migraine symptoms during initial and follow-up visits with all patients presenting with a complaint of dizziness.

Why would it be the case that vestibular migraine is present so often? No one's been able to fully explain that, except Kelsey, actually, Dr. Hatton, did a pretty great job with her discussion of MARD. But we do have folks that have suggested the fact there are common neurotransmitters. She mentioned serotonin, CGRP, glutamate that are associated with migraine pathophysiology, and which are also present in the vestibular system, that can support a dismodulation that creates shared dysfunction. She really, again, explained that quite good. It's also been noted that reciprocal connections between vestibular nuclei and the trigeminal nucleus caudalis exist. Those reciprocal connections can modulate neural activity within both the trigeminovascular system and the vestibular system. For example, trigeminal stimulation has been shown to produce nystagmus in migraine patients. So there are relationships here, but there's still no definitive answer. In conclusion, our results support and extend the work of Zhu et al. but using data generated from the perspective of the patient. The majority of patients have a single vestibular disorder. That was 68.2% in the current study. BPPV and vestibular migraine are the most common single vestibular disorders. And a significant percentage, so 32% in the current study, of patients will present with more than one

vestibular disorder. So that's kind of a much larger number to consider than the 3.7 originally discussed in Zhu et al. It's essential to consider that possibility that there could be more than one, and sometimes multiple issues going on, so we can improve assessment and management. Vestibular migraine is common, both as a single diagnosis, and also, it was the most common co-occurring diagnosis. That finding would suggest that vestibular migraine should be given strong consideration when developing a differential diagnosis, especially in more complicated cases. And finally, additional work is needed to more clearly identify why these relationships with vestibular migraine exist. So I think we do have a few minutes for some questions. I did want to let people know that we, our friends at AudiologyOnline were able to upload the Dizziness Symptom Profile and the scoring tool in the classroom as handouts if you would like to those. They're very easy to use. You just print them out. The scoring tool is an Excel file. So you would enter the data into the file, it will show you what the differential diagnosis is.

So it looks like, let me see that we... Okay, maybe Kelsey handled the question. We're, again, happy to take any questions. One of the questions that we had that Kelsey took was, in diagnosis, what are the differences between dizziness and vertigo? And so Kelsey responded with the International Classification of Vestibular Disorder definitions that dizziness is the sensation of disturbed or impaired spacial orientation without a false or distorted sense of motion, while vertigo is the sensation of self-motion of head/body when no self-motion is occurring, or the sensation of distorted self-motion during an otherwise normal head movement. So I kind of think about it like dizziness is more of an umbrella term, and then vertigo would be a very specific type of dizziness, like lightheadedness would be another type of dizziness. So that's personally how I try to differentiate those. So hopefully, that was helpful. And then there's a second comment. On the DSP, the word dizziness is used in the general sense. We do not use the word vertigo on the questionnaire anywhere, as common use of dizziness in English covers a multitude of sensations. So that was from Kelsey, I'm sure, and that, I truly agree with that as well. Vertigo is a term that, those of you that are working with

patients, I'm sure you've noticed this, that people use that term, vertigo, to account for multiple types of sensations and unsteadiness. It's many things. So that would be a word that you would probably not want to use. And we use this more generic term in DSP. So we have another question that, "I'm taking nortriptyline for disembarkment syndrome, "migraine, and dental neuralgia, and it helps. "Can you explain how this drug affects serotonin?" So I would have probably shifted that over to Dr. Hatton, since she did such an amazing job explaining that. You know, we're all audiologists. And so I'm not sure that we can give you a proper explanation of those effects on serotonin. But I'm so happy that that is working for you. And I would say that you probably do fall into the group of most people that once they identify the appropriate medication, they really do get better. They start seeing improvement. So I'm thankful for that for you. All right, and if there are no further questions, I think each of the three of us, if we have any comments, I think the comment that I would make is that I think all of us that work with patients with dizziness and imbalance, absolutely, from the evidence that you've seen here, we need to think beyond just a single diagnosis, and that certainly, I would agree that our patients often, most often would have a single diagnosis, at least that's what some of the data suggests. But there's a good, pretty large group, about 30% of patients that may have at least two, and often even more than that. So certainly, we need to consider that. And then it looks like, from Dr. Hatton, she encourages folks to look at the guidelines that are found within her references for headache, the different types of headache, vestibular classifications. There really is a great deal of excellent information out there. And then I'm reading down, and she was gonna jump in and say that. So I'm sorry, Kelsey. I stole your--

- Oh, that's okay. Yeah, it's good as audiologists, if you are very unfamiliar and uncomfortable with those territories, having the actual definitions of what is definite vestibular migraine versus probable vestibular migraine, or definite Meniere's disease versus probable Meniere's disease, these are classifications that your otology and other physician colleagues are operating on with these patients. So it's good for us to also have our hands on these. And they are public and available for everybody when it

comes to the International Classification of Headache Disorders. And with the vestibular disorders, that is published in a couple of different places. But you can look for the International Classification of Vestibular Disorders. It's very helpful to just have those definitions on hand when you're trying to explain this, not really to the patient but more to your colleagues that you'll be collaborating with in trying to manage these patients. And I think that's all the questions that we have. So Christy is gonna take over and close us out, but thanks for listening today.

- [Gary] Thank you.

- [Christy] Thank you, everyone, and have a great day.