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Response to ‘Lack of Diagnostic Value of High-Pass Noise Masking of Auditory Brainstem Responses in Meniere’s Disease by Claudia F. J. De Valck, Gerd M. E. Claes, Floris L. Wuyts, and Paul H. Van de Heyning. *Otology & Neurotology* (2007) 28:700–707.’

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In the recent paper “Lack of Diagnostic Value of High-Pass Noise Masking of Auditory Brainstem Responses in Meniere’s Disease” by De Valck et al. (2007), the authors concluded that, due to its low sensitivity (31%) and low specificity (28%), the ABR high-pass noise masking technique (Don et al., 2005), commercially known as CHAMP (Natus/Bio-logic Corp.), had “...no discriminative value in differentiating Meniere’s from non-MD subjects with otovestibular symptoms” (p. 706). In reviewing their data and analyses, we found errors that led to misleading and inappropriate conclusions. This response will briefly review the errors and suggest that once these errors are corrected, the revised values of 100% sensitivity and 80% specificity are consistent with the excellent sensitivity and specificity described in the original paper (Don et al., 2005).

Before discussing the errors, it is important to note that the authors state, “...when only definite MD patients were included, and only the interpretable tests were used, a 100% sensitivity was obtained as in the study of Don et al. (11).” (p.705) In addition, they state, “...none of our definite MD patients had a test within normal ranges.” (p. 706) Thus, as in our study (Don et al., 2005), these authors found that in all the patients with definite Meniere’s disease (MD) and measurable responses, the test results were abnormal. So, what errors led De Valck et al. (2007) to their erroneous conclusion about the value of the CHAMP test?

Error 1

More than half of the ears in the test population (18 of 32) did not have definite MD based on the standard diagnostic criteria set by the AAO-HNS guidelines (1995). Because these possible and probable MD ears may not actually have MD, they should not have been included in the sensitivity calculation.

Sensitivity is defined as the percentage of MD cases detected in a test population of patients with MD. As clinicians well know, the hallmark symptoms of MD are common to other otologic

problems. Thus, as noted in the AAO-HNS guidelines (1995): “Only patients in the definite or certain categories should be reported as having Meniere’s disease.” Yet, in their calculation of the test’s sensitivity, De Valck et al. (2007) included all 32 of the MD ears in their test population, even those classified as possible (13) and probable (5) MD ears. However, these possible and probable ears may not actually have MD. Thus, negative (normal) test results for these patients may accurately indicate the absence of MD and the authors should not have interpreted these results as false negatives (i.e., missed MD cases). Only the 14 ears classified as definite MD ears should have been included in the calculation of the test’s sensitivity.

Error 2

In 13 of the 32 MD ears and 15 of the 25 non-MD ears, the authors could not make a latency delay measurement, but they included these unmeasurable results in the sensitivity and specificity calculations instead of excluding them as “Could Not Test” or “No Response” cases.

De Valck et al. (2007) claim that for 13 of their 32 MD ears and 15 of their 25 non-MD ears, they could not make the latency delay measurement required for the test because they could not clearly identify a wave V in the 0.5 kHz high-pass response. Thus, in nearly 50% (28 of 57) of all the patients tested, they report “test not interpretable” results. In determining the sensitivity of the test to be only 31%, the authors consider the 13 unmeasurable results in the MD test population to be missed MD cases (i.e., false negatives), even though they did not measure a normal long latency delay (i.e., ≥ 0.3 ms) consistent with the absence of MD. Similarly, in determining the specificity of the test to be only 28%, the authors consider the 15 unmeasurable results in the non-MD population to mistakenly indicate the presence of MD (i.e., false positives), even though they did not measure a short latency delay (i.e., < 0.3 ms) consistent with the presence of MD. If a latency delay cannot be measured and the results still cannot be interpreted after *all* the high-pass responses have been considered in the analysis (see discussion of Error 3 below), then the results should be classified as “Could Not Test” or “No Response” cases and excluded from the sensitivity and specificity calculations. Only 7 definite MD ears and 10 non-MD ears (Table 3) had measurable results.

The reasons for the inability of the authors and their experts to read a wave V in the 0.5 kHz high-pass responses were not discussed and example waveforms were not shown. We suggest possible reasons for the lack of measurable responses in the discussion of the next two errors.

Error 3

Incomplete analyses of the high-pass responses may have led the authors to classify the outcomes for five non-MD ears with normal or near-normal hearing as “test not interpretable” results.

In non-MD subjects with normal or near-normal hearing, wave V in the 0.5 kHz high-pass response may be missed if the analysis does not include assessment of the other high-pass waveforms. In non-pathologic subjects, one observes an increase in the latency of wave V as the cochlea is progressively masked with 8, 4, 2, 1 and 0.5 kHz high-pass masking noise. However, it is quite possible not to see a clear wave V in the 0.5 kHz high-pass response because in the 0.5 kHz high-pass masking condition, most of the cochlea is masked and the response must come from the unmasked region below 0.5 kHz. Peaks from this low frequency region of the cochlea are broader and less well defined due to poorer synchronization. However, if the latency of wave V increases as the cochlea is progressively masked, then the results are *not* consistent with the presence of MD. This is true even if wave V in the 0.5 kHz high-pass response cannot be clearly identified and the latency delay cannot be calculated. The authors never showed any of their waveforms but we would surmise that in the five non-MD ears with normal or near-normal hearing (≤ 25 dB PTA) and “test not interpretable” results, one would

see a progressive latency increase in the high-pass responses. If so, then these results should have been interpreted as normal (non-MD) results.

Error 4

The authors tested patients with hearing losses close to or greater than the stimulus presentation level and included their unmeasurable results in the sensitivity and specificity calculations.

The authors report that 7 of the 14 definite MD ears and 15 of the non-MD ears had unmeasurable results (Table 3). Based on Table 5, 5 of the 7 definite MD ears and 4 of the 15 non-MD ears with unmeasurable latency delays had pure-tone averages (PTAs) of about 50 dB or greater (range 48.8 to 81.3 dB). The stimuli in the CHAMP system are presented at only 60 dB nHL. Thus, it is not surprising that there were no measurable responses in these ears with significant hearing losses. The stimuli were either near or below threshold. Proper training in the use of CHAMP warns against testing patients with PTAs around 50 dB or greater because of the likelihood of poor or absent wave V responses in some or all of the high-pass responses simply due to lack of cochlear activation by the 60 dB nHL stimuli. The authors justify their approach by stating that “...several patients with a minor hearing loss or even normal thresholds produced noninterpretable results” (page 705). This is a specious argument for applying the test in patients with significant hearing loss that could result in lack of cochlear activation. The related issues of misinterpretation of unmeasurable results (Error 2) and noninterpretable results in patients with little or no hearing loss (Error 3) have already been addressed.

Error 5

Several significant errors in the Overview of the 57 CHAMP Tests (Table 5) may indicate underlying problems that exacerbate Errors 1–4.

Rather than an exhaustive list of questions and concerns about the data in Table 5, we have selected just three to discuss. First, the authors state that “*If the latency difference was less than 0.3 ms, the test was considered indicative of the presence of cochlear hydrops.*” (p. 701) However, the result for Ear 37 is classified as positive for MD even though the latency delay is 0.5 ms. Second, the authors state they classified their MD patients into one of four diagnostic categories based on the AAO-HNS guidelines (p. 701). According to the guidelines (1995), the clinical criteria for a diagnosis of possible MD are “*Episodic vertigo of the Menier’s type without documented hearing loss, or sensorineural hearing loss, fluctuating or fixed, with dysequilibrium but without definitive episodes. Other causes excluded.*” Ear 2 is classified as a possible MD ear, but the AAO-HNS definition clearly does not apply because according to Table 5, the patient displayed all four of the hallmark symptoms of MD on the day of testing. Third, the authors state that “*Hearing was assessed using the pure-tone average at 500 Hz, 1 kHz, and 3 kHz.*” (p. 701) But according to Table 5, the mean hearing thresholds were calculated using 0.5, 1, 2, and 3 kHz. It is unclear how the mean was calculated and whether only those 3–4 frequencies, if any, were assessed on the day of testing. Note, too, the absence of a mean hearing threshold for Ear 4 and the lack of any reason for this in the text. Training with the CHAMP software should have stressed the importance of using recent and complete threshold information to assist in the accurate analyses of high-pass responses.

Error 6

In an attempt to assess the diagnostic value of the CHAMP test in a “real clinical setting”, the authors used no subject selection criteria other than the suspicion of MD.

The authors claim they wanted to assess the diagnostic value of the CHAMP test in a clinical setting (p. 703). To do so, they “...made no selection of subjects, but rather all subjects with a suspicion of MD were included, as in a real clinical setting...” (p. 705). This statement is troubling for two reasons. First, in any clinic, there should be some level of subject selection to prevent use of a test when it is clearly inappropriate. Some of the consequences of testing inappropriate subjects were presented in the discussion of Error 4 (testing patients with too much hearing loss). Second, although testing all subjects with a suspicion of MD may be appropriate in a clinical setting, as long as the recommended CHAMP test criteria (e.g., acceptable degree of hearing loss) are met, correct interpretation of the resulting outcomes is essential. Unfortunately, in their interpretation of results from subjects suspected of having MD, but not diagnosed with definite MD, it appears that De Valck et al. (2007) may have missed an important distinction between the CHAMP test and the AAO-HNS guidelines they used for categorization of their MD subjects (see discussion below). Some of the consequences of the misinterpretation of results from patients not diagnosed with definite MD were presented in the discussion of Error 1 (inclusion of possible and probable MD cases).

What happens to the sensitivity of the CHAMP test in the De Valck et al. (2007) study if we now correct the errors? Correcting Error 1 requires excluding the possible (13) and probable (5) MD ears from the MD test population, leaving just the 14 ears classified as definite MD ears. For these 14 definite MD ears, correcting Error 2 requires excluding 7 “test not interpretable” results (Table 3), leaving just 7 MD ears with interpretable results. As reported in Table 5 and noted by the authors themselves (pp. 705 and 706), the CHAMP test results for these seven definite MD ears with interpretable results are positive for MD. Thus, once Errors 1 and 2 are corrected, the sensitivity of the test increases dramatically from 31% to 100%, a sensitivity that is consistent with the claim of the original Don et al. (2005) study.

What about the specificity? Correcting Error 2 requires excluding 15 “test not interpretable” non-MD results (Table 3), leaving just 10 non-MD ears with interpretable results. Assuming the latency delays in Table 5 are correct (not the classification of the results), then only two of these non-MD ears had positive tests for MD. This means that after correcting the errors, the specificity of the test increases from 28% to 80%. Note that this calculation of specificity assumes that the positive results in the two “non-MD” ears are wrong and recall that because the hallmark symptoms of MD are shared by many other otologic problems, MD is both difficult to diagnose and difficult to rule out based on symptoms alone, especially in the early stages. Thus, instead of conclusively dismissing these positive test results as mistaken diagnoses in true non-MD ears, the authors should consider the possibility of early MD and recommend follow-up if the patients notice any change in their symptoms.

In considering some of the errors made by De Valck et al. in their 2007 study, it appears that they may have missed one important distinction between the CHAMP test and the AAO-HNS diagnostic guidelines for MD: the CHAMP test, unlike the AAO-HNS guidelines, does not have “possible” or “probable” MD result categories. The CHAMP test was developed in response to the lack of a sensitive and specific objective clinical test for MD. It assesses the presence (or absence) of cochlear hydrops and has no “possible” or “probable” outcomes, only “yes” (consistent with MD) or “no” (not consistent with MD) outcomes. Thus, the CHAMP test cannot and should not be expected to match symptoms-based AAO-HNS guideline diagnoses of “possible” or “probable” MD. Many patients with possible or probable MD diagnoses will have negative CHAMP test results because they do not actually have MD, and many patients with otovestibular symptoms but no MD diagnosis may have positive CHAMP test results because of underlying cochlear hydrops. Thus, good clinical studies of the CHAMP test should base their sensitivity calculations on patient populations with AAO-HNS guideline diagnoses of definite MD, not “possible” or “probable” MD. In addition, the best non-MD control population for specificity calculations is a group of non-MD normal-hearing subjects

because in any MD study that includes control subjects with otovestibular symptoms, there is always the possibility that some of the subjects may have undiagnosed MD.

It is important to remember that once the authors' errors are corrected, the sensitivity of the CHAMP test for the De Valck et al. 2007 study is 100% and the specificity is 80%. The 100% sensitivity is consistent with the excellent sensitivity (100%) in the 2005 Don et al. study. The 80% specificity, while not as good as the 100% specificity found by Don et al. (2005) in non-MD normal-hearing subjects, is still very good for the clinical population the authors studied. With 100% sensitivity and 80% specificity, the CHAMP test clearly demonstrates discriminative value in differentiating the authors' MD patients and non-MD subjects with otovestibular symptoms.

Because of errors, the sensitivity and specificity determined by De Valck et al. (2007) are inaccurate, and their conclusions about the value of the test are misleading. We believe their study has been a disservice to the clinical community. We welcome appropriate studies of the sensitivity and specificity of our test as they may lead to improving a test that we believe is very sensitive, specific and useful in assessing Meniere's disease.

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