I read with interest the recent article by Yelverton and colleagues that profiles a large group of patients with hearing loss and mitochondrial mutations. The authors should be commended for the size and scope of this study; however, I feel that the study’s limitations may lead to misconceptions among some readers about this interesting and important patient group.

The authors note some limitations to their retrospective study, including a lack of controls, selection bias, and incomplete clinical information. However, they do not mention that their selective screening of only MTTS1 and MTRNR1 genes may also result in bias, especially in light of a poorly defined cohort. While I agree with the authors’ assertions that these 2 genes have so far accounted for the majority of mitochondrial nonsyndromic hearing loss, it is not clear that the study’s broad inclusion criteria have excluded those with syndromic features. This has implications not only for genetics research but also for clinicians considering a mitochondrial cause for a patient with deafness. Even if the authors had excluded syndromic cases, some have argued that focusing only on MTTS1 and MTRNR1 genes may hinder the discovery of novel variants. Other approaches have uncovered at least 5 new mitochondrial genes implicated in nonsyndromic hearing loss. For the clinician, identification of additional clinical features (blindness, diabetes, ophthalmoplegia, migraine, muscle weakness) associated with mitochondrial syndromes may prompt the screening of several other mitochondrial genes. These features may or may not be present when the patient first develops hearing loss, resulting in a blurring of clinical boundaries between “syndromic” and “nonsyndromic” cases.

Second, do the authors have any explanations for the lack of matrilineal inheritance in several cases? Given the well-established inheritance pattern of mitochondrial disease, could it be that these simplex or multiplex families represent sporadic cases? Or perhaps other factors are at play, as the authors allude to in their discussion of phenotypic variability in patients harboring the A1555G mutation. Could these findings be partly explained by variable penetrance or additional mitochondrial (or autosomal) mutations not identified by this study? The role of nuclear modifiers, which would not follow a matrilineal inheritance model and alter the penetrance of mitochondrial mutations, may affect the genetic approach to diagnosis. Perhaps future studies could focus on whether the hearing loss in these patients can be attributed to mitochondrial dysfunction rather than specific mitochondrial mutations alone.

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and clinically relevant mitochondrial mutations in the goal to define the phenotypic characteristics of the common and clinically relevant mitochondrial mutations in the MTTSI and MTRNR1 genes. Verkerk et al correctly point out that our methodology did not include mitochondrial genomic sequencing in all subjects, which would limit detection of rare or novel mitochondrial variants for both nonsyndromic and syndromic hearing loss. Given the advances in next-generation sequencing technology, this would be an interesting follow-up project to pursue. Our analysis of existing repository clinical data did exclude syndromic causes, insofar as this is possible when examining a database that may contain only a single point in time at the ascertainment of the proband.

As we describe in the Discussion, both in existing literature as well as the current study, incomplete penetrance is well documented in both A1555G and A7445G mutations, with only around two-thirds of those carrying the mutation developing hearing loss. Lack of a maternal phenotype of hearing loss could be due to discrepant use of aminoglycosides, the cause of gene-environment interaction in the A1555G variant, or a lack of penetrance and variable phenotype. In general, the sporadic mitochondrial phenotype is restricted to lethal mitochondrial deletions. Many of our pedigrees also came from dense, deaf-by-deaf matings, and we did not have maternal DNA in several cases to confirm matrilineal inheritance. We agree that future research should examine the role of nuclear modifiers, additional mitochondrial or autosomal mutations, and the role of mitochondrial dysfunction in deafness.

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Reference

Possible Errors in the Article “Clinical Features of Recurrent or Persistent Benign Paroxysmal Positional Vertigo”

I read with great interest the article written by Choi et al, “Clinical Features of Recurrent or Persistent Benign Paroxysmal Positional Vertigo.” The authors demonstrated the incidence of persistent or recurrent benign paroxysmal positional vertigo (BPPV). However, there were potentially incorrect data in the article. In the Materials and Methods section of article, the authors stated, “Eventually, 120 patients were enrolled, and their follow-up was 6 months at minimum” in the last lines (lines 1-2) of the left column on page 920. In the Results section of the abstract, the authors described the following: “Among 120 patients with BPPV, 93 (77.5%) were typical, 15 (12.5%) were persistent, and 12 (10.0%) were recurrent.” The authors also showed the similar description: “Of 120 patients with BPPV, 93 (77.5%) were typical, 15 (12.5%) persistent, and 12 (10.0%) recurrent (Figure 1)” in the first paragraph of the Results section of text on page 921. However, the corresponding case numbers (percentages) accounting for 3 types of BPPV were shown as “Typical BPPV 98 (58.3%), Persistent BPPV 15 (8.9%), and Recurrent BPPV 12 (7.1%)” in “Figure 1. The incidence of persistent or recurrent benign paroxysmal positional vertigo” on page 921. It seems that the data in figure 1 is incorrect. Therefore, I recommend that the authors correct any possible errors in the article.

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