severely affecting the high frequencies. Furthermore, hearing impairment in the USA I family seemed to start with higher thresholds in the lower frequencies. In contrast to the other families, some of the affected members in the Belgian and both American families reported tinnitus [1–6]. All families attained a severe to profound hearing loss by the age of 70. It is likely that hearing is congenitally impaired, especially at the high frequencies. Previous reports mentioned substantial intrafamilial variation in onset age or offset level, but annual threshold deterioration was almost uniformly calculated at approximately 1 dB/year [6, 9, 11–15]. Most *KCNQ4* mutation carriers required a hearing aid from between 10 and 40 years onwards. Vestibular testing was described in 37 members of the Dutch I family and 11 members of the Dutch IV family and revealed increased vestibulo-ocular reflex activity in approximately 30% of the cases [11, 14]. In addition, speech recognition scores had been analyzed in 45 members of the latter Dutch families [13, 14]. Given the level of pure-tone impairment, they presented with relatively good scores. Moreover, the scores did not deteriorate substantially before the third decade of life and progressed at a relatively low rate.

Discussion and Conclusions

In general, a certain genotype-phenotype correlation can be recognized in the studied DFNA2/*KCNQ4* families. The Belgian family with its purely high-frequency loss represents one exception. Their deviant phenotype could be the result of their specific type of mutation (inactivating), which is probably responsible for a reduced quantity (50%) of normal *KCNQ4* channels (haploinsufficiency). In contrast, all other known mutations lead to a (stronger) dominant negative effect with the formation of some normal (1/16) and a large majority of dysfunctional channels [9]. Further research is necessary to confirm this theory and thus confirm the existence of a true phenotype-genotype correlation.

In conclusion, DFNA2/*KCNQ4*-related hearing impairment involves symmetrical, high-frequency hearing impairment, progressive for all frequencies and probably starting from an early age onwards.

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