Diabetes mellitus and auditory brainstem responses

Sir,

I read the recent publication on diabetes mellitus and auditory brainstem responses with a great interest. Gupta et al., concluded that “BERA is a simple, non-invasive procedure to detect early impairment of acoustic nerve, and CNS pathways, even in the absence of specific symptoms.” I would like to make a discussion on this work.

I agree that there can be the aberration of the auditory system in DM. However, the suggestion to use the BERA as a possible screening tool has to be systematically evaluated. The first question is on the cost effectiveness of this technique. Before possible implementation of routine usage of BERA for general diabetic patients, this point has to be clarified.

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Sequencing MODY1-6 genes in Uyghur Early-onset diabetes pedigree

Sir,

Maturity-onset diabetes of the young (MODY) is a monogenic form of diabetes mellitus characterized by autosomal dominant inheritance, early age of onset, and pancreatic beta cell dysfunction. With advancement in genomic technology, at least 11 distinct MODY genes have been identified to date and more are believed to exist.

The prevalence of Type 2 diabetes was 8% in China and 8.16% in the Uyghur population; the cause of high prevalence is unknown. There is no prior study of the molecular genetics of early-onset Type 2 diabetes in Xinjiang and there is no report on mutations in MODY genes in the Uyghur ethnic population. We had undertaken the study to screen for mutations and polymorphisms in six known MODY genes in a Uyghur probable MODY family.

We collected two Uyghur early-onset diabetes pedigrees from Kashikar city of Xinjiang Uyghur Autonomous Region. We clinically diagnosed one pedigree as a probable MODY family according to the MODY criteria. Two cases (Participants II.1 and III.2) from a family were involved in this research with their informed consents. Genomic DNA was isolated. All exons and flanking intron regions of HNF-4α, GCK, HNF-1α, IPF-1, HNF-1β, and NEUROD1 genes were amplified from a genomic DNA sample by polymerase chain reaction (PCR). All sequences were analyzed and compared with the reference sequence from NCBI with the Lasergene software (DNASTAR, Wisconsin, USA). Changes in the sequence were checked against published polymorphisms and mutations from the Human Genome Variation Society (HGVS, http://www.HGVS.org).

The six MODY genes represent an excellent candidate gene set for identification of genetic variation in the MODY...
Seventeen sequence variations were identified and none of them were classified as pathogenic mutation. Sequence variants of HNF-1α gene were relatively more common [Figure 2]. HNF-1α exon7 p.Gln497Gln and NEUROD1 Exon1 c.164G>A were novel variations. Others were previously described common polymorphisms. No pathogenic mutations or polymorphisms were found in GCK.

A Chinese study suggested that the S487N, I27L variants might be associated with Type 2 diabetes mellitus (DM) in Chinese subjects, but these variants’ significance in the development of Type 2 DM needs to be further investigated.[8] In this study, we also sequenced the S487N, I27L variants of the HNF-1α gene. A recent study suggested that variants of MODY genes can enhance the risk of susceptibility to Type 2 DM.[5]

In summary, this is the first report in which six known MODY genes were screened for mutations in the Uyghur ethnic group. Moreover, in the thorough analysis of the six MODY genes we did not identify any HNF-1α risk haplotype in this family, while HNF-4α, GCK, HNF-1ß, IPF-1 and NEUROD1 apparently failed to contribute to the etiology of early-onset diabetes in this Uyghur family, providing further support for the high heterogeneity of this disease.

This is the first step of our researches on the MODY genes in a Uyghur probable MODY family. These variations which were identified in this study may indicate a relatively higher susceptibility to MODY or Type 2 DM in the Uyghurs.

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