



Huntington's disease-like 2 in South Africa

To the Editor: Huntington's disease (HD) is a late onset, autosomal dominant neurodegenerative disorder characterised by progressive movement impairment, affective disturbance and cognitive dysfunction. In 2001, Huntington's disease-like 2 (HDL2) was identified.¹ The causative factor in both disorders is due to a repeat expansion mutation but these occur in two distinct genes: the *IT15* gene (chromosome 4p16.3) for HD and the *JPH3* gene (chromosome 16q24.3) for HDL2.

In a recent pilot study, 63 individuals of either black African (BA) or coloured ancestry (also referred to as mixed ancestry – MA) who were previously found not to carry the HD-causing expansion following routine testing by the University of Cape Town (UCT)'s National Health Laboratory Services (NHLs) laboratory, were screened for the HDL2 disease-causing

expansion. Eight individuals from 4 families were found to have the CTG-repeat expansion, ranging in size from 41 to 60 repeats. Three of these families were of BA origin and one was an MA family.² In our preliminary haplotype studies to ascertain the origin of the HDL2 mutation, a common core haplotype was inferred for the BA and MA groups.

The aim of this letter is to raise awareness among clinicians and neurologists in South Africa that HDL2 is present in the South African population. Interestingly, in contrast with HD which is found predominantly in Caucasian individuals, HDL2 has been found worldwide exclusively in individuals of BA ancestry.³ The current perception is that HDL2 should only be considered in individuals whose recent ancestors are of BA descent, but we have shown that in South Africa it is also present in the MA population, and could therefore be missed. Awareness should therefore be raised that HDL2 should not only be considered in BA individuals.

It is also clear from the literature and from our experience that many HDL2 patients do not manifest with chorea, but present with variants of a rigid-akinetic syndrome.⁴ Similarly, MRI features may be atypical when compared with HD, with greater evidence for damage to the striatum in HDL2.

We therefore propose that a diagnosis of HDL2 should be considered in a wide spectrum of neuropsychiatric and abnormal movement presentations. A molecular diagnostic test for HD and HDL2 is now available to test simultaneously for both conditions at the UCT NHLs laboratory. It is anticipated that identification of more HDL2 patients from diverse populations will broaden the phenotypic description of this apparently rare disorder.

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