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Huntington disease (an unpublished epidemiological study)

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Huntington's disease (HD) is an autosomal dominant, progressive neurodegenerative disorder which bears excessive repetition of CAG tri-nucleotides in the *HTT* gene. When the number of such repetitions reaches a certain level, the protein encoded by this gene, huntingtin (htt), undergoes a structural change as a result of the increased number of glutamine residues. Numerous studies have investigated the origin of the disease by correlating haplotypes of the *HTT* region to ethnicity. Many SNPs are highly sensitive markers of disease chromosomes and have stronger linkage associations with expanded CAG. These disease-associated SNPs constitute a cluster of similar haplotypes: haplotype A was found in a vast majority of affected chromosomes. The majority of HD chromosomes in Europe contain haplotype A and East Asian populations (China and Japan) haplotype C. The aim of this study was to investigate the genetic diversity of the *HTT* gene expanded alleles (>35 CAG), intermediate alleles (27–35 CAG), and control alleles (<27 CAG) in Brazilian patients and unaffected individuals. Affected and unaffected samples from 33 Brazilian HD pedigrees were tested for genetic markers associated with the A1 *HTT* haplotype (European and Amerindian A1 SNPs), following the methodology suggested by Kay et al., 2015. Concerning the HD chromosomes, 52% of HD families were classified in haplo-group A1. In contrast, haplo-group A1 accounted for only 5% of chromosomes of the Brazilian general population (<27 CAG). Haplo-group C was present in approximately 22% of the normal chromosomes but only in 6% of the HD chromosomes. The HD chromosomes had an average size of 44 (39 to 62) CAG repeats, and the normal chromosomes had 17 (14 to 30). The families included in the A1 haplo-group were also tested for the presence of a specific SNP which distinguished A1 Amerindian from A1 European. Only three HD families belonged to A1 Amerindian haplo-group, whereas the others to the A1 European. CAG expansion in European populations does not occur randomly, but is associated with specific *HTT* haplotypes (A1 and A2). There is no treatment for HD except palliative therapy; therefore silencing the HD mutant allele is an attractive strategy for future intervention because it would target the cause of HD. HD allele-specific silencing is important in order to preserve wild-type *HTT* function. Haplotype searching can play an important role in order to identify Brazilian patients who could benefit the allele-specific silencing in the future.

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