LETTER

''Devolution'' of bipedality

Ozcelik *et al*. (1) report mutations in very-low-density lipoprotein receptor (VLDLR) that are associated with quadrupedal gait. They propose a pivotal role for VLDLR in the transition from quadrupedal to bipedal locomotion in man. VLDLR is a key regulator of cerebellar development in vertebrates (2). All VLDLR mutations reported to date result in disequilibrium syndrome (DES) with cerebellar hypoplasia and are neuroanatomically indistinguishable (1, 3, 4). In contrast to the Turkish population reported by Ozcelik *et al*., Hutterites carrying a complete deletion of VLDLR are bipedal (3). Ozcelik *et al*. hypothesize that the Hutterites are more severely afflicted because of a chromosomal deletion and that this causes loss of motor skills required for quadrupedal locomotion, thereby forcing them to habitually walk upright. Quadrupedal locomotion in individuals with cerebellar hypoplasia has been proposed to define a distinct genetic syndrome of "human devolution" or "reverse evolution" ("Unertan syndrome") (5).

Clinical, evolutionary, and molecular evidence refutes their hypothesis. Quadrupedal locomotion is more likely an adaptation to the severe truncal ataxia present in all VLDLR-deficient patients, resulting from a combination of uneven, rough surfaces in rural areas, imitation of affected siblings, and lack of supportive therapy. Conclusions about the role of VLDLR in the transition from quadrupedal to bipedal locomotion are uninterpretable and untenable in the presence of such extensive structural cerebellar defects. Quadrupedal gait is thus likely an epiphenomenon caused by neurodevelopmental malformation and ataxia combined with unfavorable environmental conditions and does not define a separate genetic entity. A more informative and appropriate name for VLDLR deficiency in disequilibrium syndrome would be DES-VLDLR.

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