Debrisoquine hydroxylation polymorphism in Leber's hereditary optic neuropathy

Leber's hereditary optic neuropathy (LHON) causes severe visual loss, most commonly in young men. The primary genetic defect is a mutation in mitochondrial DNA in the tRNA(Leu) gene (mtDNA) at position 3460, causing the substitution of a cytosine to a thymine (C to T) in the wild type (C = 3460 bp, T = 3460 bp).

Mutations reported in these alleles are common in index cases of families with LHON. Forty percent have been found in a large sample of patients with LHON. The CYP2D6 G to A transition and base pair deletion were analysed in two separate polymerase chain reactions using, respectively, oligonucleotide primer pairs C + D and E + F as previously described. Genotypes and allele frequencies in patients and controls were compared by \( \chi^2 \) analysis with Yates' correction for \( 2 \times 2 \) tables.

There was no excess of mutant CYP2D6 alleles in affected LHON index patients compared with unrelated controls; nor was there an excess of poor metabolisers (table). It is therefore unlikely that impaired debrisoquine metabolism is responsible for the development of LHON in patients with a pathogenic mtDNA mutation. Apart from exposure to or impaired metabolism of environmental toxins, there are other possible explanations for the development of blindness in LHON. Firstly, the excess of affected males has led to suggestions that an X linked visual loss susceptibility locus may be involved. Secondly, some features of LHON are surprising for a genetic condition and an autoimmune component has been suggested. This is supported by the finding that, in rodents, mtDNA encoded antigens can act as transplantation antigens.

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Pure sensory stroke caused by cortical infarction associated with the secondary somatosensory area

Pure sensory stroke, described as a distinct clinical entity in 1965 by Fisher, denotes a hemisensory disturbance without other neuroanatomical deficits. Although pure sensory stroke occurs usually due to lacunar infarcts, it can be caused by lesions involving any portion of the common human sensory pathway from the postcentral gyrus, known as the primary somatosensory area (S1), to the thalamus and cerebellum. We report a patient with pure sensory stroke resulting from a cortical infarction on the inner bank of the parietal operculum, which is known as the secondary somatosensory area (S2).

A 44-year-old right-handed man with a history of cigarette smoking was admitted because of sudden decrease of touch and pain sensation in his right hemibody. On admission, neurological examination disclosed normal motor function and reflexes. There was a moderate hypaesthesia for light touch, pain, and temperature senses on the right side including the face, oral cavity, arm, trunk, and leg. Discriminative touch, joint, and vibratory sensation as well as stereognosis and graphesthesia were preserved on the right side. Cranial nerve function including taste sensation were within normal limits. There were no neuropsychological signs such as aphasias, impairment of calculating ability, or disturbance of right-left discrimination. Magnetic resonance imaging taken four days after the onset showed a cortical infarction located within the inner bank of the left parietal operculum (figure). The common sensory pathway from the postcentral gyrus to the medulla, especially the thalamus, was normal on MRI. Results of routine laboratory examinations and vasculagrams were unrevealing.
Two somatosensory projection areas, S I and S II, have been shown to exist in the brains of mammals and humans. In primates, a region, located in the postcentral gyrus, is especially concerned with the integration of sensory experience and with the discriminative qualities of sensation. S II has been mapped to the parietal operculum in many animal species, including humans. According to recent studies with monkeys, the cortical area defined as S II lies limited to the inner bank of the parietal operculum, which is smaller in size than previously considered. The organisation of S II in humans remains unclear, although it has been considered as a cortical focus for pain perception. Penfield and Jasper initially identified an S II in humans in the parietal lobe and contributed to somatic sensation. They also reported that no sensory disturbances occurred in patients after ablating S II. Conversely, the parietal operculum and its projections in the cortex produce various sensory disturbances such as impairment of all sensory modalities, impaired cortical sensation, or decreased pain and temperature sensation. The best of our knowledge, there are no prior studies describing cortical infarction of a limited area in the inner bank of the parietal operculum.

There have been reports of pure sensory stroke due to lesion along the common human sensory pathway including parietal cortical infarctions of S I. This patient showed restricted sensory impairment in light touch, pain, and temperature senses of the entire right side and fulfilled the criteria of pure sensory stroke. This sensory dysfunction seems to have resulted from a circumscribed cortical infarction on the inner bank of the contralateral parietal operculum, presumably S II.

Possible cortical overlap between postencephalitic parkinsonism and progressive supranuclear palsy

Encephalitis lethargica is a transmissible disease of the CNS which occurred as a pandemic between 1916 and 1928 and subsequently very few sporadic cases have been reported. Close neuropathological similarities exist between postencephalitic parkinsonism and progressive supranuclear palsy, although the clinical presentation is quite different. In postencephalitis lethargica, Parkinson's disease, and progressive supranuclear palsy in childhood, development of parkinsonism and later, progressive neurological disability, including frequent falls, neck extension, and supranuclear down gaze palsy. Despite the direct involvement of the ventromedial and lateral gaze evoked nystagmus, but neither were found in the presence of an optokinetic nystagmus. Vestibulo-ocular function tests showed a deviation of the eyes towards the side of the gaze and an optokinetic nystagmus, but no nystagmus was seen. Caloric testing showed large amplitude responses in the horizontal plane, with no evidence of horizontal gaze nystagmus, but no nystagmus was seen. Bilateral irrigation at 20°C for 40 seconds resulted in three minutes of pronounced upbeat nystagmus, whereas bilateral irrigation at 44°C showed pronounced downbeat nystagmus lasting four minutes. Auditory brainstem evoked potentials showed waves of small amplitude with bilateral delay of wave III and V consistent with eighth nerve or intrinsic brainstem dysfunction. Brain CT with 40% at 0.5 Hz and 35% at 0.5 Hz and 40% was carried out. Progressive supranuclear palsy predominantly affects the saccadic system; vestibular and optokinetic stimuli typically produce a tonic drift of the eyes in the direction of the slow phase of the induced response with no saccadic intrusions to produce a positive nystagmus. Postencephalitis lethargica.

Coronal T2 weighted MRI showing a high signal intensity as a cortical area in the inner bank of the left parietal operculum.
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