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 and is associated with abnormalities in the inner mitochondrial respiratory chain such as cytochrome P-450 and alcohol dehydrogenase.1-3 Patients with LHON have a high frequency of mutations in the mitochondrial genome, which can be transmitted from mothers to sons. The LHON gene is located on the mitochondrial DNA and is inherited maternally.

Several groups have identified mutations in the mitochondrial genome that are associated with LHON. These mutations are found in the noncoding region of the mitochondrial genome, and they are thought to cause abnormal expression of the mitochondrial genes. The most common of these mutations is a G to A transition in the tRNA-Ser(UGA) gene, which is located on chromosome 19. This mutation is responsible for the majority of cases of LHON and is found in approximately 70% of patients with LHON.

The significance of these mutations is not fully understood. It is thought that they lead to the production of a dysfunctional mitochondrial protein, which is thought to be responsible for the loss of retinal ganglion cells. However, other factors may also be involved in the pathogenesis of LHON, such as environmental factors, such as alcohol and tobacco, and oxidative stress.

There have been several case reports of patients with LHON who have also had a history of smoking or alcohol use. These patients have been found to have a higher frequency of mutations in the mitochondrial genome than non-smokers or non-drinkers. This suggests that environmental factors may play a role in the development of LHON.

It is not clear whether the mutations in the mitochondrial genome are the only factor involved in the pathogenesis of LHON. Other factors, such as age, gender, and family history, may also be important.

In conclusion, LHON is a rare but important cause of irreversible blindness. It is thought to be caused by a mutation in the mitochondrial genome, and it is inherited maternally. The significance of these mutations is not fully understood, and more research is needed to determine the role of environmental factors in the development of LHON.

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

Two somatosensory projection areas, S I and S II, have been shown to exist in the brains of mammals. They are discernible in humans, as well as 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 locus for pain perception. Penfield and Jasper initially identified an S II in human brains as a source of producing various sensory disturbances such as impairment of all modalities, impaired cortical sensation, or decreased pain and temperature sensation. To 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 lateral parietal operculum, presumably S II.

Possible clinical 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 few sporadic cases have been reported. Close neuropathological similarities exist between postencephalitic parkinsonism and progressive supranuclear palsy although the clinical presentation is quite different. Postencephalitic parkinsonism in children, developed parkinsonism and later, progressive neurological disability, including frequent falls, neck extension, and supranuclear down gaze palsy. Despite the existence of progressive supranuclear palsy on clinical examination, the neuro-otological investigations showed some distinctive features. In 1917, aged six years, the patient was diagnosed as having "sleepy sickness", from which he seemed to recover fully. In 1959, 42 years after his encephalitis lethargica, he began to have excessive sleepiness such that he might fall asleep while playing cards or when at work. At about the same time, he was also noted to have inarticulate speech and a resting tremor of his right hand and oculo-yractic crises occurred. Three years later he developed mild rigidity and walked with a "parkinsonian gait". Brain CT scans showed no evidence of lesions, but a search for spongiform change was negative. The left eyeball started it a small dose of levodopa with benefit. In 1979, aged 68, he began to fall and developed troublesome blepharospasm, with impairment of extracocular movements. In 1981, he had a further oculoplastic crisis, after an excessive dose of sinemet. In 1986, he was readmitted to the National Hospital for Neurology and Neurosurgery for further investigation. His postural reflexes were severely impaired. He was extremely slow to initiate gait, but once started he could walk fairly flusently and with only mildly reduced steps. A general poverty of facial expression and bradykinesis, together with a resting tremor of the lower jaw and right hand were noted. There was pronounced axial rigidity with neck extension, but power, coordination, and limb reflexes were normal, with the exception of absent ankle jerks and extensor plantar responses. Speech was slow and monotonous. The pupils were pinpoint, but circular in shape, and reacted briskly to both direct and consensual light. There was a mild bilateral Babinski. Pronounced blepharospasm triggered by glabellar tapping, together with increased facial jerks, were noted.

Neuro-otological examination disclosed smooth pursuit eye movements in the horizontal plane of about 30° to 40° to both right and left, but only 10° upwards and no downward pursuit from the midsagittal. Doll's head manoeuvres significantly improved both the horizontal and vertical eye movements, indicating supranuclear involvement. Volitional saccades were absent in the vertical plane, whereas slow, stepped saccades were elicited to about right and left of the midposition. There was no convergence and no spontaneous or positional nystagmus. Optokinetic nystagmus showed a good response to clockwise and occipital beats on counterclockwise stimulation, but there was no response in the vertical plane. Horizontal eye movements were recorded with conventional DC electro-oculography. Hypometric, slow saccades were noted downhill nystagmus lasting four minutes, particularly at the lowest frequency (0.2 Hz; peak velocity 20°/s), but at higher frequencies and velocities, there was a symmetric large reduction of smooth pursuit function (gain 40% at 0.2 Hz and 30% at 0.4 Hz and 40°s). Small, dysrhythmic, but preserved optokinetic responses were found on both clockwise (gain 82%) and counter clockwise (gain 77%) stimulations. The responses included an extremely fast supranuclear and lateral gaze evoked nystagmus, but neither were found in the presence or absence of optic fixation. Vestibulo-ocular function tests showed a deviation of the eyes to the left with evidence of gaze movement, but no nystagmus was seen. Caloric testing showed large amplitude responses in the horizontal plane, with no development of the rotatory component of optic fixation. Bilateral irrigation at 20°C for 40 seconds resulted in three minutes of pronounced upbeat nystagmus, whereas bilateral irrigation at 44°C showed profound downbeat nystagmus lasting four minutes. Audiatory brainstem evoked potentials showed waves of small amplitude with bilateral delay of wave III and V consistent with eighth nerve or intracranial brainstem dysfunction. TETSYOHI HORIUCHI

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