LETTERS TO THE EDITOR

The thermolabile variant of 5,10-methylenetetrahydrofolate reductase is not associated with Parkinson's disease

Oxidative damage has been suggested as a potential mechanism for both atherosclerosis and neurodegenerative disorders such as Parkinson's disease.1 One report has noted a 2-5-fold increased risk of cardiovascular disease among patients with Parkinson's disease,2 suggesting that a common genetic variant may contribute to both diseases. One such candidate genetic factor, the ApoE4 allele, is found at a raised frequency in those with cardiovascular disease and Alzheimer’s disease, but was recently shown not to be raised in patients with Parkinson’s disease.3

Homocysteine is a pro-oxidant that acts via the copper catalyst, oxygen dependent, production of hydrogen peroxide. Moderately raised concentrations of the amino acid homocysteine (mild hyperhomocysteinemia) confer a twofold to threefold risk of vascular disease. In a significant proportion of cases mild hyperhomocysteinemia arises from the interaction of the homoyzogous thermolable (t) genotype of 5,10-methylenetetrahydrofolate reductase (MTHFR) with suboptimal folate and B12 nutrition.4 The t genotype has also been directly associated with cardiovascular disease.5 We therefore determined the prevalence of the t genotype in patients with Parkinson’s disease. Patients with a known or occult Parkinson’s disease (n = 188) and matched controls (n = 184) were selected as described previously.6 Cases had initial symptoms before the age of 56 years, and were born after 1924. Controls were age and frequency matched by five-year bands, sex, and urban/rural indicator. Genotyping for the t allele was performed by polymerase chain reaction and Hinf1 digestion of genomic DNA extracted from whole blood.7 The t genotype was present in 9.6% (n = 18) of the patients with Parkinson’s disease and 7.1% (n = 13) of the controls. In the Parkinson’s disease group the heterozygote frequency was 42.5% (n = 80) and the non-thermolable homozygote frequency was 47.9% (n = 90). The corresponding frequencies in the control group were 47.3% (n = 82) and 45.6% (n = 84) respectively. There was no significant difference in the frequency distribution of genotypes (χ2 = 1.26, 2df, P = 0.33) and the odds ratio for the t genotype was 1.39 (95% confidence interval 0.63-3.12).

These results clearly indicate that the t genotype is not associated with Parkinson’s disease and does not explain the finding that patients with Parkinson’s disease are at increased risk of vascular disease. The fact that no association is found may indicate that the brain is protected from raised homocysteine concentrations by the preferential accumulation of folate in the CNS, where its concentration is three times that found in serum. Other genetic candidates should be examined for a potential role in oxidative damage, and the importance of common environmental factors such as dietary antioxidants considered.

Dawning L HARMON DOROTHY RAMSBOTTOM JAMES T WHITEHEAD Genetics Department, Trinity College, Dublin 2, Ireland

Yoad BEN-SHLOMO GEORGE DAVEY-SMITH Department of Clinical Medicine, University of Bristol, UK

Correspondence to: Professor AS Whitehead, Genetics Department, Trinity College, Dublin 2, Ireland.


Refsum’s disease: long term treatment preserves sensory nerve action potentials and motor function

Refsum’s disease is a recessively transmitted disorder characterised by retinitis pigmentosa, polyneuropathy, and cerebellar ataxia associated with tissue storage of phytanic acid.8 Nerve conduction studies in patients with Refsum’s disease show abnormal motor nerve conduction velocity (NCV) with signs of chronic denervation.9 Sensory nerve action potentials were usually abnormal and absent.10 We present a patient with Refsum’s disease with preservation of SNAPs and motor functions after 20 years of continuous treatment with a diet restriction and plasmapheresis. Her initial clinical course has been reported.11

A 39 year old woman with retinitis pigmentosa and cataracts was admitted in 1976 with a four week history of paraesthesia and weakness. Physical examination showed exfoliative dermatitis, constricted visual fields, right ptosis, and facial diplegia. She had bilateral foot drop and decreased sensation distally. She was areflexic. The peroneal nerves were palpably enlarged at the fibular heads. Protein content of CSF was 210 mg/dl with normal cell count and glucose. Nerve conduction studies showed reduced motor conduction velocity of the right peroneal nerve (21-1 ms) and of the right median sensory conduction velocity (4-4 ms). Sural nerve biopsy showed an increase in the number of small myelinated and unmyelinated fibres. In the right median sensory nerve, the distal sensory amplitudes were 340 μV, and the proximal sensory amplitudes were 100 μV. The sensory nerve action potential was not present at the wrist and was absent at the elbow. Phenytoin, an anticonvulsant and antidepressant, was given but the patient continued to have worsening motor and sensory involvement.

Two weeks after admission, all nerve conduction studies were performed. A 39 year old woman with retinitis pigmentosa and cataracts was admitted in 1976 with a four week history of paraesthesia and weakness. Physical examination showed exfoliative dermatitis, constricted visual fields, right ptosis, and facial diplegia. She had bilateral foot drop and decreased sensation distally. She was areflexic. The peroneal nerves were palpably enlarged at the fibular heads. Protein content of CSF was 210 mg/dl with normal cell count and glucose. Nerve conduction studies showed reduced motor conduction velocity of the right peroneal nerve (21-1 ms) and of the right median sensory conduction velocity (4-4 ms). Sural nerve biopsy showed an increase in the number of small myelinated and unmyelinated fibres. In the right median sensory nerve, the distal sensory amplitudes were 340 μV, and the proximal sensory amplitudes were 100 μV. The sensory nerve action potential was not present at the wrist and was absent at the elbow. Phenytoin, an anticonvulsant and antidepressant, was given but the patient continued to have worsening motor and sensory involvement.

The beneficial effects of dietary treatment and plasmapheresis in Refsum’s disease are established.12 The effectiveness of the treatment can be monitored by recording the plasma phytanic acid concentrations. However, not all of the clinical findings in Refsum’s disease are reversible.13 Rapidly developed weakness associated with an acute exacerbation often responds more rapidly and completely to treatment than a gradual onset polyneuropathy. The acute flaccid tetraparesis of our patient responded quickly to plasmapheresis. The weakness did not improve since it is likely due to chronic polyneuropathy.

In conclusion, a predominently motor axonal polyneuropathy may be seen in Refsum’s disease and long term dietary
treatment and plasmapheresis are effective in preserving sensory nerve potentials and motor function.

JAU-SHIN LOU
ROBERT SNYDER
ROBERT C GRIGGS
Department of Neurology,
University of Rochester Medical Center,
Rochester, NY, USA

Correspondence to: Dr Jau-Shin Lou, University of Rochester Medical Center, Department of Neurology, Box 673, 601 Elmwood Avenue, Rochester, NY 14642, USA.


Contraversive visual tilt illusion associated with a cerebellar infarction

Visual tilt illusion consists of an abnormal perception of the environment, which seems to be rotated at a variable angle without any change in the other characteristics of the objects. It is sometimes associated with other postural and ocular tilt effects. It can be secondary to disturbances in the peripheral or central vestibular pathways.1-7 Previous studies suggest that cerebellar injuries could also cause it,1 but this has not been documented before. We report a case of visual tilt illusion probably associated with an isolated cerebellar lesion, studied with CT and MRI.

A 56 year old man with hypertension and hypercholesterolaemia had a sudden attack of continuous vertigo not related to cephalic movements, with nausea and vomiting and a deviation to the left while walking. When it disappeared, 48 hours later, he complained that he saw objects as if they were tilted to his right by 30° and they should be rotated antieclockwise—that is, to his left—so as to be perceived as vertical. He had a slight head and body tilt to his left that worsened when he was asked to close his eyes and stand upright. There was no skew deviation or other ocular motor disorders. Fundal photographs were not taken, so that ocular torsion could not be assessed. There were no other alterations on neurological examination. Two weeks later the patient was asymptomatic. Brain CT and MRI showed a right hemispheric cerebellar lesion, suggesting an ischaemic infarction (figure). No brainstem or cortical alterations were found.

Visual tilt illusion has been described in unilateral peripheral vestibular lesions; in brainstem injuries, typically in the Wallenberg syndrome, in other medullary and mesencephalic lesions, and in thalamic and parietoinsular cortex disorders.2-12 The most frequent conditions associated with visual tilt illusion are vascular lesions.1 As far as we know, there are no reports on documents of abnormally ordered sensory injuries associated with the illness.

Physiologically, the vestibular pathways make contact with the ocular motor system, the spinal cord, and the vestibular cortex, contributing to the stabilization of posture and perception of verticality and self-motion.1-5 The tonic bilateral vestibular input builds up the actual central vestibular tone in the three major planes: horizontal or “yaw”, sagittal or “pitch”, and frontal or “roll”.1-5 It seems that central pathways that mediate vestibular function in either of the three planes travel independently of each other, so that a specific lesion could cause a disorder restricted to one of them.1 The vestibular tone in the frontal or “roll” plane allows a correct perceptual, ocular, and postural alignment to the “gravitational vertical”; an imbalance in this tone causes a lateral tilt with alteration in perception of verticality, head and body posture, misalignment of the visual axes, or ocular torsion.1-5 Patients perceive the surroundings and their body as if they were tilted in the opposite direction to what the CNS erroneously computes as being vertical and try to adjust the visual objects and posture to it. Dieterich and Brandt showed that an alteration in the perceived verticality is not just the sensory consequence of the rotation of the eyes, as they can appear separately and are not proportional in degree.1 Furthermore, it is possible that not all the effects of tilt occur in one patient, and the perceptual disorder itself is the most sensitive sign of a vestibular tone imbalance in the frontal plane.1,3 Brainstem structures that mediate the vestibular tone in the “roll” plane include the vestibular nuclei and the interstitial nucleus of Cajal—perhaps the most rostral structure related to the control of vertical and torsional head and eye position. Both are connected by the medial longitudinal fasciculus, which crosses the midline in the pons.1,5 Vertical visual tilt is, then, ipsiversive to peripheral or pontomedullary lesions and contraversive to pontomesencephalic lesions and, in both cases, is usually associated with other tilt effects; in most rostral lesions it may be either ipsiversive or contraversive and is usually isolated.1,3 The role of the vestibular cerebellar structures with respect to the control of subjective verticality is not well known at the moment.2

Our patient’s clinical findings suggest that he had an inclination of the internal representation of the gravitational vector to his left and he tried to adjust both visual objects and posture to what he perceived as being vertical. It would have been interesting to assess whether there was overt ocular torsion to define his clinical setting more exactly, but it makes no difference to interpretation as ocular torsion can be associated or not with perceptual or other tilt effects.1 Our patient showed a right hemispheric cerebellar ischaemic lesion, in a territory dependent on the posteroinferior cerebellar artery (PICA), with no mass effect and no brainstem or other alterations on MRI. His perceptual and postural tilt was contraversive to the lesion. It is possible that an additional subtle medullary lesion in the distribution of the PICA, not evident with clinical and imaging studies, produced the tilt effect. This may be because, the major infratentorial arteries supply both brainstem and cerebellum and it is very difficult to differentiate the effects of cerebellar and brainstem lesions.1 But the tilt should then be ipsiversive to the hypothetical lesion. Therefore it is not likely that an associated medullary ischaemia could cause the tilt effects in our patient. A mesencephalic injury could cause this clinical picture but there should be other brainstem symptoms and MRI was normal at this level. A supratentorial disorder is unlikely because there were no MRI alterations and there were associated postural tilt effects. In this patient, we think that cerebel lar dysfunction could be responsible for the tilt effects.

The present report confirms a previously hypothesized role for the cerebellar structures in the control of perception of verticality,2 and may contribute to a better knowledge of the pathophysiology and the topographic diagnosis of the central vestibular syndromes.

M BARON
JM GILARDO
M LOUSA

Servicio de Neurología, Hospital Ramón y Cajal, Universidad de Alcalá de Henares, Madrid, España

Correspondence to: Dr M Baron, Servicio de Neurología, Hospital Ramón y Cajal, Ctra de Colmenar, Km 9.100, 28034 Madrid, Spain.


Low striatal D2 receptor binding as assessed by [123I]IBZM SPECT in patients with writer’s cramp

Writer’s cramp is a form of idiopathic focal task specific dystonia. In accord with other studies on idiopathic and symptomatic dystonia, Tempel and Perlmutter suggested the presence of an abnormal striatal dopaminergic circuitry drive in writer’s cramp.1 In view of the

Downloaded from http://jnnp.bmj.com/ on April 30, 2016 - Published by group.bmj.com
Refsum's disease: long term treatment preserves sensory nerve action potentials and motor function.

J S Lou, R Snyder and R C Griggs

*J Neurol Neurosurg Psychiatry* 1997 62: 671-672
doi: 10.1136/jnnp.62.6.671-a