of hormonal failure; spontaneous recovery can occur. Prospective studies clarifying the natural history of hypopituitarism associated with head trauma and allowing the development of appropriate guidelines for the follow up and management of these patients are needed.

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REFERENCES

- 1 **Benvenga S**, Campenni A, Ruggeri RM, *et al.* Hypopituitarism secondary to head trauma. *J Clin Endocrinol Metab* 2000;**85**:1353–61.
- 2 **Kelly DF**, Gaw Gonzalo IT, Cohan P, *et al.* Hypopituitarism following traumatic brain injury and aneurysmal subarachnoid hemorrhage: a preliminary report. *J Neurosurg* 2000;**93**:743–52.
- 3 **Aimaretti G**, Ambrosio MR, Di Somma C, *et al.* Traumatic brain injury and subarachnoid haemorrhage are conditions at high risk of hypopituitarism: screening study at 3 months after brain injury. *Clin Endocrinol* 2004;**61**:320–6.
- 4 **Agha A**, Rogers B, Sherlock M, *et al.* Anterior pituitary dysfunction in survivors of traumatic brain injury. *J Clin Endocrinol Metab* 2004;**89**:4929–36.
- 5 **Agha A**, Sherlock M, Phillips J, *et al.* The natural history of post-traumatic neurohypophyseal dysfunction. *Eur J Endocrinol* 2005;**152**:371–7.
- 6 **Lamberts SWJ**, de Herber WW, van der Lely A. Pituitary insufficiency. *Lancet* 1998;**352**:127–34.

An aspirin responsive non-progressive chronic chorea

Chronic generalised chorea is a physically and socially disabling symptom with few effective treatments. We present a case of long standing neurologically isolated non-progressive chorea which resolved almost completely after the introduction of aspirin therapy.

Case report

A 41 year old female presented with chronic generalised chorea since she was 10 years old. Onset had been over several weeks and was preceded by recurrent sore throats. There was no family history of neurological disease.

Since onset, the chorea had fluctuated slightly over time but had never progressed or resolved. It was slightly worse during the patient's menstrual periods but was severely disabling during her pregnancies. Her first pregnancy ended with an intra-uterine death after 31 weeks. Her second pregnancy ended as a miscarriage after 8 weeks. A third pregnancy resulted in a son being delivered at 34 weeks. However, the chorea had become so severe during this pregnancy that the patient decided to undergo sterilisation. Between pregnancies, the chorea settled back to its previous levels.

Over the years, the following investigations were negative or normal: clotting studies, haemoglobin, white cell count, C-reactive protein, erythrocyte sedimentation rate, serum urea and electrolytes, liver function tests, creatinine kinase, lactate, protein electrophoresis, thyroid function tests, amino acid profile, white cell enzymes, antistreptolysin O titre, C₃ and C₄ complement, serum caeruloplasmin and urinary copper, blood film for acanthocytes, syphilis serology, rheumatoid factor, autoantibody screen, anti-cardiolipin IgG and IgM, anti- β_2 -glycoprotein-I IgG and IgM, anti-basal ganglia antibodies, genetic testing for mitochondrial encephalopathy with lactic acidosis and stroke-like episodes (MELAS), chest x ray, ECG, EEG, CT and MRI brain, and nerve conduction studies. A low platelet count of $106 \times 10^9/l$ (normal range: 150–400) was noted during the first pregnancy and persisted thereafter. Giant platelets on the blood film and bone marrow biopsy changes were consistent with peripheral platelet consumption.

At the age of 41 the patient presented to the neurology clinic because she still found that the chorea was interfering with her daily life. She had generalised bilateral chorea affecting her arms, legs, tongue, and speech. Higher cognitive function was intact. Previous treatments had been of little or no benefit. Tetrabenazine and diazepam provided some improvement. Propranolol and sulpiride had no effect. A trial of steroids (prednisolone 60 mg) seemed to improve her chorea for 2 weeks but had to be discontinued due to intolerance of the adverse effects.

She was commenced on aspirin 75 mg each morning because of the suspicion of antiphospholipid syndrome (APS), although antibody testing was repeatedly negative. This resulted in a marked immediate improvement in her chorea, such that it became almost unnoticeable. She noticed that the chorea appeared to return towards the end of the day. She was advised to stop treatment during menstruation because of heavy periods. However, stopping the aspirin was also associated with a return of the chorea towards the end of the week. The aspirin was increased to 150 mg once a day. The chorea disappeared almost completely at all times of the day. This improvement has been maintained for over 2 years. She tries not to stop taking aspirin for longer than 1 week in case the chorea returns.

Discussion

We report the case of a patient with long standing chorea which improved after aspirin was given. In a literature review we found only one previous case of chronic chorea that had been reversed with aspirin alone.¹

We suspect our patient has APS because of the history of chorea, miscarriages, placental thrombosis, and thrombocytopenia. However, none of the laboratory criteria are met and therefore a definitive diagnosis cannot be made.

Seronegative APS patients are described and are presumed to have other, as yet unidentified, circulating antibodies causing thrombosis.² Alternatively, it is possible that the patient has persistent Sydenham's chorea (SC), although throat swabs and the antistreptolysin O titre were both normal at presentation and anti-basal ganglia antibodies were negative. However, anti-basal ganglia antibodies are positive in only ~69%

of chronic SC which does not usually respond to aspirin.³

APS and SC are both thought to be antibody mediated. In APS, antiphospholipid antibodies may affect phospholipid binding proteins causing hypercoagulability. However, antibodies in APS may also activate endothelial cells and up regulate adhesion molecules, cytokines, and prostacyclins. This generates an inflammatory vasculopathy, resulting in ischaemic injury with microthrombosis to the basal ganglia. There is also laboratory evidence of APS antibodies binding directly to the brain.⁴

Aspirin is widely used in APS for its presumed antiplatelet properties. Activated platelets have been observed in APS with neurological manifestations but not in patients without neurological features. However, aspirin also inhibits the formation of inflammatory cytokines. Aspirin has been shown to down regulate prostaglandin E₂, which is produced by brain endothelial cells in vitro, and prostacyclin receptors have been identified in the striatum. It has also been shown to exert a protective effect on endothelial brain cells by decreasing leucocyte adhesion molecule expression at the cell surface.⁵ In the absence of a measurable coagulopathy, these mechanisms may explain the benefit of aspirin therapy in our patient. Alternatively, the aspirin may have a modulatory platelet effect independent of endothelial cells.

While it could be argued that aspirin therapy coincided by chance with an improvement in the chorea, this seems unlikely. The patient had chronic chorea for 30 years and her symptoms never improved spontaneously as they did immediately after starting aspirin. A placebo effect is unlikely as other treatments had provided no significant benefit. Moreover, her chorea returns if she does not take the aspirin for a week. However, she is unwilling to stop taking aspirin for longer and we believe it would be unethical to advise this. To address the question definitively, a multi-centre randomised controlled trial would be required, but this might be impractical in such an uncommon condition.

In conclusion, aspirin may be useful in the treatment of some patients with chronic non-progressive chorea.

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Patient consent: the patient gave her written informed consent. However, we have not included any identifying details in this case report.

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References

- 1 **Hodges JR**. Chorea and the lupus. *J Neurol Neurosurg Psychiatry* 1987;**50**:368–9.
- 2 **Hughes GRV**, Khamashta M. Seronegative antiphospholipid syndrome. *Ann Rheum Dis* 2003;**62**:1127.
- 3 **Harrison NA**, Church A, Nisbet A, *et al.* Late recurrences of Sydenham's chorea are not associated with anti-basal ganglia antibodies. *J Neurol Neurosurg Psychiatry* 2004;**75**:1478–9.

- 4 Lampropoulos CE, Hughes GRV. The antiphospholipid (Hughes') syndrome: changing the face of neurology. *Eur J Intern Med* 2004;15:147–150.
- 5 Dunoyer-Geindre S, Kruihof EK, Boehlen F, et al. Aspirin inhibits endothelial cell activation induced by antiphospholipid antibodies. *J Thromb Haemost* 2004;2:1176–81.

A third eye for the surgeon

Neurologists and engineers have developed a new camera system for surgeons, which looks where the eyes look. This innovative device uses voluntary and reflexive eye movements, which are registered in 3-D by video-oculography and then computed online, as signals to drive the camera servo motors in three planes: yaw, pitch, and roll (fig 1). Its primary objective is to allow a freely mobile user to aim the optical axis of a head mounted camera system at the target(s) at which he/she is voluntarily looking in the visual field, while the ocular reflexes stabilise any image shaking by naturally counter rolling the “gaze in space” of the camera during head and visual scene movements and during locomotion. The biological system of the human ocular motor control incorporates these functions, but so far, no camera system has combined free user mobility with image stabilisation and unrestricted exploration of the visual surround.

As biological and technical systems are governed by closely related physical laws, their sensorimotor control mechanisms are similar. The biological principles that have evolved over millions of years continue to

serve as inspiration for new technical constructions. Here the human ocular motor system is exemplary. Visual exploration is made possible by the use of voluntary saccades when the eyes are quickly moved from one visual target to another, and voluntary smooth pursuit, when the eyes follow a moving target. The vestibulo-ocular reflex relies on inner ear sensors that signal both linear accelerations and angular head velocities to the brain. This velocity information is transformed mathematically by integration into a positional signal, which is then inverted and delivered to the eye muscles.^{1,2} During head movements, the biological reflex moves the eyes in their orbits in the opposite direction to the head motion, thus ensuring a stable projection of the visual scene onto the retina. A similar mechanism becomes active when large field visual stimuli are moved in front of an observer (optokinetic reflex).

This complex ocular motor system also controls the orientation of the optical axis of the novel head mounted camera. To prevent perception of apparent motion of the visual scene (oscillopsia) during rapid eye and camera movements, an artificial saccadic suppression mechanism can be incorporated, which is triggered by saccade onset. This artificial motion suppression can be achieved by repeating (“freezing”) the last frame acquired before saccade onset for the duration of the camera saccade. Depending on the saccade amplitude, the image has to be frozen for about 100 ms.

Thus, the surgeon using this camera can move his/her head and eyes during image acquisition without having to fear image shaking artefacts, while at the same time continuously document an operation. In addition, the vergence angle of the eyes delivers valuable information for a possible autofocus functionality, as the vergence angle directly depends on the distance from the observed object.

There are numerous commercially available head referenced scene cameras combined with an eye tracker that highlights the visual target in the scene image. However, all of these systems possess a head fixed camera that does not move with the eyes. Their field of view is restricted by the optics, and therefore the visual target is not always in the range of the scene camera. In contrast, the novel system described here covers the whole explorable field of view and therefore the camera documents every eye movement of the surgeon, for example, when he/she is looking down. The image centre captured by the scene camera coincides with the surgeon's foveal fixation, assuming there is accurate calibration of eye tracker and scene camera. The current system has an accuracy of 0.45 degrees, which is well within the 2 degrees of the foveal area.

Several medical and non-medical applications are conceivable for the camera during free locomotion:

- analysis of the ocular exploratory behaviour of freely mobile test persons or patients, for example, to assess the development of gaze control from childhood to adulthood or abnormal visual exploration in psychiatric or neurological disorders,
- animal films that correlate behaviour with visual control,
- sports newscasts showing the viewpoint of the sportsman in action,

- analysis of stimuli that control gaze for advertisement purposes,
- night vision tasks in which the user enjoys mobility while preserving his field of view and continuing watching, for example, a thermal picture projected onto the half transparent infrared mirror.

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References

- 1 Robinson DA. The use of control system analysis in the neurophysiology of eye movements. *Ann Rev Neurosci* 1981;4:463–503.
- 2 Glasauer S, Dieterich M, Brandt T. Central positional nystagmus simulated by a mathematical ocular motor model of otolith-dependent modification of Listing's plane. *J Neurophysiol* 2001;86:1546–54.

Interaction between dopamine β -hydroxylase and interleukin genes increases Alzheimer's disease risk

Healy and colleagues¹ recently reported that dopamine β -hydroxylase (DBH) activity could mediate predisposition to Parkinson's disease through its role in catalysing the conversion of dopamine to noradrenaline (norepinephrine). By studying a promoter variant (–1021 C/T) in the DBH gene which has been shown to influence plasma DBH activity, they showed that homozygosity for the low DBH expressing T allele was protective against Parkinson's disease, and proposed that lower levels of DBH protein might lead to increased ratios of dopamine to noradrenaline.¹ In Alzheimer's disease, significant reductions in noradrenergic neurones within locus coeruleus, as well as reduced brain noradrenaline levels, have often been reported.² In addition, there is a causative link between reduced noradrenaline content and the potentiation of β -amyloid (A β) induced cortical inflammation.³ We hypothesised that relative noradrenaline deficiency associated with homozygosity for the (–1021) DBH T allele might lead to increased risk for Alzheimer's disease, either through an independent effect or through interaction with the proinflammatory interleukin (IL) 1A and IL6 genes.

The study involved 266 patients with Alzheimer's disease (68% women; mean

Figure 1 The user is wearing a head mounted device equipped with video eye trackers. They consist of two laterally attached infrared video sensors and two infrared mirrors, one in front of each eye, which reflect the images of the eye to the sensors. The image information is transmitted to a video-oculography computer, which uses image processing algorithms to determine the three dimensional eye positions. The eye position is transformed into a signal for servo motors that control the optical axes of a rotatable head fixed camera system. Because the infrared mirrors of the eye movement detectors are transparent to visible light, the user's field of view is not restricted. Thus, the axis of the “third technical eye” is always aligned to the axes of the user's eyes. Consent was obtained for publication of this figure.