cedent infection or the non-specific elevation of the antibody titre due to poly-
clonal activation of the memory B cells, there remains a possibility that this virus triggered the immunological derangement of this unusual case.

KICHIRO MATSUMURA* MANABU SAKUTA* TOMOYUKI IKARI† KUMIKO JITSUKAWA‡ Department of Neurology,* Department of Medicine,† Department of Dermatology,‡ Japanese Red Cross Medical Center, 4-1-22 Hiroo, Shibuya, Tokyo 150, Japan.

References
3 Grover RW. Transient acantholytic der-
4 Bystyn J. Immunofluorescence studies in tran-
sient acantholytic dermatosis (Grover's dis-
5 Atkins CJ, Kondon Jr JJ, Quismorio FP, Friou
GJ. The choroid plexus in systemic lupus ery-
6 Koss MN, Chernack WJ, Griswold WR, Mcintosh RM. The choroid plexus in acute serum sickness. Morphologic, ultra-
7 Grundke-Iqbal I, Lassman H, Wisniewski

Accepted 22 September 1987

Visual evoked potentials and neopterin: biop-
terin ratios in urine show a high correlation in
Alzheimer's disease

Sir: Tetrahydrobiopterin is the rate controlling co-factor in the synthesis of the neurotransmitters dopamine and nor-
adrenaline.1 Alzheimer's disease is associ-
ated with decreased tetrahydrobiopterin levels,2-5 through the reduced conversion of dihydropterin triphosphate to tetra-
hydrobiopterin.6 Analysis of postmortem cerebrospinal fluid,7 postmortem temporal cortex8 and serum of patients8 with Alzheimer's disease has shown that an
elevated neopterin: biotin (N:B) ratio is a measure of this reduced conversion rate.

In Alzheimer's disease, measurement of the visual evoked potential (VEP) has shown that the major positive, or P2, component of the flash VEP is delayed, while the P100 component of pattern reversal VEP is unaffected.9 10 This unusual combination of results is believed to indicate that the pathol-
ogy is at the level of the visual association areas. Subtraction of the latency of the pat-
tern reversal P100 component from the flash
P2 component, therefore gives a value which is elevated in Alzheimer's disease. The mag-
nitude of this flash-pattern latency difference has been shown to increase with increasing severity of dementia.11 12

Ten patients suffering from Alzheimer's disease were diagnosed and referred for the study by a consultant psychogeriatrician.
All were diagnosed as presenting with pri-
mary dementia of the Alzheimer type with no evidence of cerebrovascular disease. All had significant memory loss but were capable of fixing pattern reversal stimulus and providing a urine sample. The degree of dementia was moderate. Urine samples, taken directly into ascobic acid to give a final ascobic acid concentration of 1%, were measured for neopterin, biotin and creatinine.12 Flash and pattern visual evoked potentials (VEPs) were recorded.10 The mean age of the patients was 77 years (standard deviation 8-21 years). The nine controls were paid volunteers, with a mean age of 81 years (standard deviation 4-39 years) with a binocular visual acuity of 6/9 or better and a Royal College of Physicians mental test score of 29/34 or better.13 14 Ophthalmoscopy was carried out on all patients and controls and a medical history obtained. No one with evidence of opthal-
mic pathology or diseases affecting the immune system was included as these would affect the pattern VEP and neopterin:
biotin ratios respectively.

The table shows that the mean values of N:B ratio, flash P2 latency and flash-pattern difference were all significantly elevated in the group with Alzheimer's disease compared with the controls. The relationship between the urine and VEP results was investigated by the determination of the corre-
table.

<table>
<thead>
<tr>
<th>N:B ratio</th>
<th>Flash P2 latency (ms)</th>
<th>Flash P2-pattern P100 difference (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alzheimer's disease (± SD) n = 10</td>
<td>2.43 ± 1.56</td>
<td>156.7 ± 17.1</td>
</tr>
<tr>
<td>Control group (± SD) n = 9</td>
<td>1.51 ± 0.62</td>
<td>136.6 ± 7.3</td>
</tr>
<tr>
<td>T test: statistical significance</td>
<td>p &lt; 0.05</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>Correlation with N:B ratios</td>
<td>0.83 (p &lt; 0.01)</td>
<td>0.92 (p &lt; 0.001)</td>
</tr>
</tbody>
</table>

Letters

Hamon CG B† Catteell RJ* Wright CE† Wychri J† Blair JA* Harding GF† Departments of Molecular Science* and Vision Sciences†, Aston University, Aston Triangle, Birmingham B4 7ET, UK Barnsley Hall Hospital,‡ Bromsgrove, UK

References
1 Leeming RJ, Rheasant AE, Blair JA. The role of tetrahydrobiopterin metabolism in neuro-
2 Leeming RJ, Blair JA. The effects of patholog-
ic and normal physiological processes on biopterin derivative levels in man. Clin Chim
3 Aziz AA, Leeming RJ, Blair JA. Tetrahydro-
biopterin metabolism in senile dementia of the Alzheimer type. J Neurol Neurosurg
4 Barford PA, Blair JA, Eggar CS, Hamon CGB, Morar C, Whitburn SB. Tetrahydro-
biopterin metabolism in the temporal lobe of patients dying with senile dementia of the
5 Williams AC, Levine RA, Chase TN, Loven-
berg W, Calne DB. CSF hydroxylysine co-
6 Anderson JA, Hamon CGB, Armstrong RA,
Blair JA. Tetrahydrobiopterin metabolism in normal brain, senile dementia of the
7 Morar C, Whitburn SB, Blair JA, Leeming RJ, Wilcock GK. Tetrahydrobiopterin metabo-
lism in senile dementia of the Alzheimer type.
We also confirmed such a spontaneous reversal of ptosis even during examination. Neurological examination did not reveal other muscle weakness except for that of the left eyelid closure. The intravenous administration of 5 mg edrophonium resulted in a paradoxical reversal of ptosis. The elevation of the eyebrow was also reversed (fig). She did not receive any anticholinesterase medication.

Patient 2 was an 11 year old girl who had developed left ptosis, diplopia and photophobia since the age of 5 years. Neurological examination at the time of onset revealed bilateral ptosis and left pseudointernal nuclear ophthalmoplegia. These signs were relieved by edrophonium injection. Furthermore, the cold test also alleviated her ptosis. Prednisolone therapy (20 mg every other day) improved her ocular symptoms moderately. At the age of 11 an exacerbation of left ptosis and limited ocular movement developed following physical exertion. She was aware that her right eyelid was ptotic when she awoke in the morning and that soon after the ptosis shifted from right to left spontaneously. By the intravenous administration of 2 mg edrophonium, her left eyelid became rather retracted and her ptosis shifted from left to right. She did not receive any anticholinesterase medication. The intravenous methylprednisolone pulse therapy led to a marked improvement of her ocular abnormalities.

Worsening of ptosis after the injection of edrophonium has generally been considered to be a negative response. Reversal of ptosis was interpreted as follows: the ptotic eyelid developed retraction and the normal eyelid became ptotic. In our patients, however, the eyelid which became ptotic after the edrophonium injection was not normal but was the affected one which drooped early in the morning and after a short sleep. Spontaneous shift of ptosis could be explained by Hering's law of bilateral and equal levator innervation: fatigability of one eyelid was greater than that of the other, thus resulting in spontaneous ptosis of one eye and the other eyelid became seemingly normal because of the central compensation for the ptosis.

When the edrophonium test was performed at this point, its effect was more prominent on the eyelid with an active lesion, leaving the other eyelid with a relatively inactive lesion ptotic. The edrophonium-induced eyelid retraction in patient 2, possibly associated with increased presynaptic ACh release to compensate for the impaired AChR prior to the test, may partially be responsible for the contralateral eyelid descent by Hering's law. The ptosis of our patients was not induced by an overdose of anticholinesterase since they received no oral anticholinesterase medication. We believe that the present observation may provide one of the plausible explanations for the edrophonium-induced reversal of myasthenic ptosis.

ATSUSHI KOMIYAMA
KEIZO HIRAYAMA
Department of Neurology,
Brain Research Institute,
Chiba University School of Medicine,
Inohana 1-8-1 Chiba 280,
Japan.

References

Paradoxical reversal of ptosis in myasthenia gravis by edrophonium administration

Sir: Paradoxical responses, worsening and reversal of ptosis, in myasthenia gravis can sometimes be seen following administration of edrophonium chloride (Tensilon), but their precise mechanisms are not fully understood. We report two patients with ocular myasthenia gravis whose ptosis reversed paradoxically by the intravenous administration of edrophonium, and discuss the possible mechanisms.

Patient 1, a 44 year old woman, had a left severe ptosis which developed about a year after thymectomy. Both anti-acetylcholine receptor (AChR) antibody and anti-striational antibody tests were positive. Early in the morning she always found her right eyelid transiently ptotic, which later in the day became seemingly normal, and left severe persistent ptosis developed.
Visual evoked potentials and neopterin: biopterin ratios in urine show a high correlation in Alzheimer's disease.

C G Hamon, R J Cattell, C E Wright, O Wychrij, J A Blair and G F Harding

*J Neurol Neurosurg Psychiatry* 1988 51: 314-315
doi: 10.1136/jnnp.51.2.314

Updated information and services can be found at: [http://jnnp.bmj.com/content/51/2/314.citation](http://jnnp.bmj.com/content/51/2/314.citation)

**Email alerting service**

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

**Notes**

To request permissions go to: [http://group.bmj.com/group/rights-licensing/permissions](http://group.bmj.com/group/rights-licensing/permissions)

To order reprints go to: [http://journals.bmj.com/cgi/reprintform](http://journals.bmj.com/cgi/reprintform)

To subscribe to BMJ go to: [http://group.bmj.com/subscribe/](http://group.bmj.com/subscribe/)