Sustained downgaze in coma after cardiac arrest

Sustained downgaze eye deviation is occasionally associated with lesions affecting the dorsal midbrain, usually thalamic haemorrhage. In stuporous or comatose patients, however, this downgaze does not necessarily indicate structural pretectal damage. Subarachnoid haemorrhage, seizure, hepatic failure, hypoglycaemia, intoxication with sedative drugs, and hypoxic encephalopathy can cause this eye sign in comatose patients. We report on three comatose patients who showed sustained downgaze after cardiac arrest. The paper concentrates particularly on the temporal neuro-ophthalmological profile.

Between January and December 1998 we examined three patients with sustained downgaze. All three patients underwent brain CT and EEG while sustained downgaze was present (table 1). Brain MRI was performed only in patient 2, 2 weeks after admission. All patients were in a comatose state after cardiac arrest, responding only to painful stimuli. Deep tendon reflexes were slightly increased in patient 1 but normal in patients 2 and 3. Flexor plantar reflexes were elicited in all patients. Cardiac arrest was due to anaphylaxis in patient 1, cardiac arrest in patient 2, and ventricular fibrillation in patient 3. Arrest time ranged from 10 to 30 minutes before resuscitation. All patients had not received any sedative drugs.

Sustained downgaze deviation was recognised in each patient when the eyelids were raised after a period of 1 to 4 days, when the immediate post-resuscitation threat of death had subsided. Horizontal oculocephalic responses were present in all patients, and the eyes could be driven upward with vertical oculocephalic manoeuvres. The pupils were normal in size and showed normal reactions to light. In patient 1, high frequency horizontal head shaking during the period of sustained downgaze may be a result of diffuse CNS damage due to diastolic dysfunction of the left ventricle. In patient 2, such transition suggests clini-

Our three patients experienced acute onset coma as a result of diffuse CNS damage after cardiac arrest. The EEG results in our patients suggested the existence of diffuse, severe brain damage. The pinto-pong gaze seen in patient 1 also implied severe bilateral cerebral damage. The sustained downgaze appeared in our patients 1 to 4 days after resuscitation. That was also the time at which patients were emerging from the most critical postevent stage. In a previously reported patient with hypoxic encephalopathy, downgaze was recognised after 2 weeks of coma. These findings suggest that sustained downgaze is not an eye sign in dying patients but that it appears in patients reaching an early recuperation stage. This notion is supported by our finding that the pinto-pong gaze changed from a smooth to a saccadic pattern before appearance of the sustained downgaze in one patient; such transition suggests clini-

Keane reported sustained upgaze deviation after cardiac arrest. Our present findings indicate that sustained downgaze may also be associated with hypoxic encephalopathy after cardiac arrest. The most striking difference between the sustained upgaze reported by Keane and sustained downgaze is the time of appearance; sustained upgaze appears immediately after cardiac arrest whereas sustained downgaze is recognised after a few days. The temporal relation between the upgaze or downgaze and pinto-pong gaze confirms this difference as pinto-pong gaze is reported to appear after resolution of sustained upgaze, whereas it preceded sustained downgaze in our patient. Keane speculated that the sustained upgaze deviation after cardiac arrest resulted from hypoxic cerebellar dam-

More than one anatomical site or physiological mechanism may well be involved in forced downgaze in comatose patients after cardiac arrest, and the mechanical details of this state are still unclear. However, it is important to recognize that downgaze can appear transiently a few days after cardiac arrest and resuscitation.

Table 1 Clinical data of the patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Cause of cardiac arrest</th>
<th>Latent period (days)</th>
<th>Duration (days)</th>
<th>Associated sign(s)</th>
<th>EEG findings</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/68/F</td>
<td>Anaphylaxis</td>
<td>10</td>
<td>2</td>
<td>5</td>
<td>Transient upward eye deviation after head shaking</td>
<td>Delta-theta waves</td>
</tr>
<tr>
<td>2/22/M</td>
<td>Cardiomyositis</td>
<td>15</td>
<td>4</td>
<td>2</td>
<td>Rigidity and dorsiflexion of the neck</td>
<td>Low voltage fast activity</td>
</tr>
<tr>
<td>3/70/M</td>
<td>Ventricular fibrillation</td>
<td>30</td>
<td>1</td>
<td>3</td>
<td>—</td>
<td>Suppression burst</td>
</tr>
</tbody>
</table>

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Priprotein gene polymorphism and Alzheimer's disease: one modulatory trait of cognitive decline?

Although its main biological function is still unknown, the prion protein gene (PRNP) has been associated with poor performance in cognitive tests in a large cohort of aged, non-demented, French people. Accordingly, this polymorphic gene represents a candidate marker for an association with Alzheimer's disease, a dementia disorder characterised by neuronal degeneration and synaptic loss. To assess whether the PRNP V/M codon129 polymorphism—alone or in combination with polymorphisms in the apolipoprotein (APOE) and interleukin (IL)-1β genes, already shown to be associated with Alzheimer's disease—alters the occurrence or clinical features of the disease, we performed a case-control study in a cohort of Italian patients with sporadic Alzheimer's disease and age matched healthy controls.

Venous blood was collected from 212 Italian patients (130 women, 82 men; mean (SD) age at disease onset 68.3 (8.0) years) affected by clinically probable Alzheimer's disease, and in MM carriers were compared by non-parametric rank sum test and their association with disease duration was assessed by the Spearman correlation coefficient.

The PRNP allele and genotype frequency did not differ significantly between patients with Alzheimer's disease and controls (allele frequency: p=0.06; 3x2 genotype frequency: p=0.12). The V allele conferred a non-significant OR for Alzheimer's disease of 0.71 (95% confidence interval (95% CI) 0.48–1.06; p=0.09; p for trend of the V allele in Alzheimer's disease=0.04). Moreover, PRNP allele and genotype frequency were not affected by sex (p=0.18 in Alzheimer's disease and 0.28 in controls), APOE e4, or IL-1β TT carrier status (data not shown).

Stratification of the Alzheimer's disease cohort by age at disease onset showed that, although not significantly, V+ genotype carriers were more represented among patients with early onset (47%) than those with late onset (37%), resulting in an OR for early onset disease due to the carriage of the V+ genotypes of 1.46 (95% CI 0.85–2.69; p=0.02). However, a Kaplan-Meyer analysis failed to confirm this differential distribution among patients with Alzheimer's disease, indicating that if an association existed, it was small. When we compared patients with early onset patients and late onset disease with their respective age matched controls, we found that the V+ genotypes were associated with an OR for Alzheimer's disease of 0.92 (95% CI 0.48–1.74; p=0.8) in the younger age group (<65 years), and 0.95 (95% CI 0.38–1.04; p=0.07) in the older age group (>65 years; allele frequency: p=0.03, genotype frequency: p=0.04, table 1).

As expected, MMSE scores showed a negative correlation with duration of Alzheimer's disease (r=-0.38, p=0.0001), but not with PRNP genotypes (p=0.08). Interestingly, despite a comparable education level (mean number of years in school: V=7.41, MM=7.52) and a similar median MMSE score recorded at the time of blood collection (15.1 in V+ and 15.3 in MM), V+ carriers had a median disease duration 9 months shorter than MM carriers (38 vs 47 months; p=0.038), possibly indicating a faster deterioration rate in V+ patients.

In conclusion, we failed to detect a significant association between the PRNP codon 129 polymorphism and the progression of sporadic Alzheimer's disease in Italy, irrespective of APOE and IL-1β genotype status, age, or sex. Combarros et al recently reported similar results in another southern European population of comparable size. However, our results suggest that patients with Alzheimer's disease carrying at least one V allele might have an earlier onset of the disease and a small but significant acceleration in their cognitive decline when compared with MM carriers. This is not a surprise as, in multigenic diseases, selected characteristics of the natural history of the disease seem more prone to be influenced by gene polymorphisms than mere occurrence of disease.

In conclusion, two independent studies have now provided evidence against PRNP as a susceptibility gene for sporadic Alzheimer's disease. Our study, however, suggests a possible modulation of disease activity due to the PRPN codon 129 polymorphism. A longitudinal assessment of a large cohort of patients with Alzheimer's disease using a full battery of reliable cognitive tests might be necessary to confirm our finding.

This work was supported in part by Telethon, Italy, by a grant from Italian MURST (40% and 60%), and by the Associazione per la Ricerca sulle Demenze (ARD). We thank Dr L. Caputo, G. De Bellis, and I Biunno for caring for patients and assistance in collecting data and Mrs Liliana Zaccherelli for excellent secretarial work.

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Table 1 PRNP 129 genotype and allele frequency in patients with Alzheimer's disease (AD) and healthy controls (HC)

<table>
<thead>
<tr>
<th>Sex</th>
<th>n</th>
<th>F</th>
<th>M</th>
<th>MM</th>
<th>MV</th>
<th>VV</th>
<th>PRNP 129 allele frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>--------------------------</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>126 (59)</td>
<td>73 (35)</td>
<td>13 (6)</td>
<td>0.77</td>
</tr>
<tr>
<td>Total sample: AD</td>
<td>212</td>
<td>130</td>
<td>82</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HC</td>
<td>201</td>
<td>120</td>
<td>81</td>
<td>103 (51)</td>
<td>78 (39)</td>
<td>20 (10)</td>
<td>0.71</td>
</tr>
<tr>
<td>Subjects &lt;65 y: AD</td>
<td>72</td>
<td>45</td>
<td>27</td>
<td>38 (53)</td>
<td>29 (40)</td>
<td>5 (7)</td>
<td>0.73</td>
</tr>
<tr>
<td>HC</td>
<td>91</td>
<td>26</td>
<td>65</td>
<td>48 (53)</td>
<td>43 (58)</td>
<td>8 (9)</td>
<td>0.72</td>
</tr>
<tr>
<td>Subjects ≥65 y: AD</td>
<td>140</td>
<td>85</td>
<td>55</td>
<td>89 (63)</td>
<td>44 (31)*</td>
<td>8 (6)*</td>
<td>0.79</td>
</tr>
<tr>
<td>HC</td>
<td>110</td>
<td>51</td>
<td>59</td>
<td>55 (50)</td>
<td>43 (39)*</td>
<td>12 (11)</td>
<td>0.70</td>
</tr>
</tbody>
</table>

*p=0.044, PRNP 129 V+/M allele frequency in AD vs HC at age matched. **p=0.03, PRNP 129 V/M allele frequency in AD at age matched with HC.
Complex musical hallucinosis in a professional musician with a left subcortical haemorrhage

Auditory hallucinosis consists of abnormal auditory perceptions that occur in the absence of a corresponding acoustic stimulus while the patient is aware of their non-real nature. Musical hallucinosis represents a particular type of acoustic hallucinosis, in which the auditory perception is formed by music, sounds, or noise. It is frequent in psychiatric diseases and is sometimes reported in sensory neural deafness, but rarely after stroke.

A 35 year old, right handed man was admitted to our department in July 1999 7 days after the onset of a slight clumsiness of his right hand followed by complex auditory perceptions. The patient had attended a symphonic concert where an orchestral transcription of Wagner's “Siegfried” was played: the patient is a connoisseur of music and a composer. When he returned home, about 1 hour later, his musical hallucinosis started. Auditory perceptions were described by the patient as a symphonic piece of music played by an orchestra with numerous kettledrums and percussion instruments. It was a rather familiar music, unknown to him, but similar to what he had heard during the concert. The theme was played in major tonality with frequent use of drums and other percussion instruments interspersed with string instruments. A chorus played by string instruments accompanied the theme. The patient said that the music reminded him of a piece by the late German romantic authors (for example, Mahler, Bruckner, and Wagner's latest works). The music was initially low in intensity but progressively increased; it was perceived in the middle of his head as if he was listening with headphones on. Conflicting emotions occurred: he felt that it was the most frightening and terrifying music he had ever heard and strongly desired to push it out of his mind but, on the other hand, he was deeply fascinated and said that he would like to compose such an exciting piece.

The patient said that during his musical hallucinosis he was able to speak, watch and understand television programs and to go about his normal activities. He reported that during the phenomenon his hearing was normal and he could hear everything going on around him, as well as the noise outside the house (for example, from the road) and all the usual noise going on in his own house.

The musical hallucinosis lasted about 90 minutes and afterwards the patient fell asleep; he did not have musical hallucinosis during the next day on awakening and it did not recur during the next 20 months.

Seven days after the episode the patient was admitted to our department. On admission a neurological examination evidenced inhibitory fibres run from the auditory cortex to lower structures of the central acoustic pathway (medial geniculate nucleus and inferior colliculus) and presumably modulate acoustic perception. The comparison of brain MRI (fig 1 A) and of a corresponding anatomical drawing (fig 1 B) suggests that the lesion just touches the acoustic radiation between the left medial geniculate body and the auditory cortex. Another explanation of such peculiar findings in our patient may derive from a recent hypothesis regarding musical hallucinosis in acquired deafness: the subcortical lesion may have caused either a disconnection between the primary auditory and the association cortices or an impairment of the “neural networks for perceptions and imagery of sounds, including the auditory association and the frontal cortex”. Indeed, the closeness of the lesion to the superior temporal gyrus may interfere with the associative fibres connecting the auditory cortex to the other cerebral areas involved in musical perceptions.

Compared with previously reported cases, our patient presents several peculiarities. Firstly, the duration of musical hallucinosis was shorter and the auditory perceptions were heard bilaterally and not lateralised in the opposite ear. Secondly, it occurred in the absence of sensory-neural deafness and might be related to a lesion involving the central acoustic pathway, even at a hemispheric level. This is not in agreement with the notion that complex acoustic hallucinosis is invariably related to damage to the peripheral acoustic pathway or to combined central and peripheral dysfunction. Thirdly, our report greatly supports the role of the dominant hemisphere in musical processing, by contrast with the accepted notion that musical perception is a specific function of the non-dominant hemisphere.

We can speculate that the musical training of the patient might have determined the shift of musical representation from the non-dominant to the dominant hemisphere.

Finally, several features of musical hallucinosis in our patient are fascinating. The similarity between the acoustic perceptions and the symphonic music that he had previously heard leads to the hypothesis of an involvement of acoustic memory circuits. The professional experience and the personal sensitivity towards symphonic music might both have contributed in the determination of musical hallucinosis influencing the processing of musical sensations.

Figure 1 (A) T1 weighted brain MRI and (B) anatomical drawing of the coronal MRI images. An area of altered signal (hypointense in centre and hyperintense at periphery), consistent with a haemorrhagic lesion, involves the left putamen and the external capsule and just touches the acoustic radiation. Comparison between the images outlines the strict relation between the haemorrhagic lesion and the acoustic radiation (double arrows) that runs from the medial geniculate body (single arrow) to the acoustic cortex in the superior temporal gyrus.

only a slight motor impairment of the right hand. His hearing sensation was normal on clinical and instrumental examination. No signs of drug or alcohol misuse were evident. Moreover there was no history of psychiatric disorders.

A cranial CT showed a small hyperdense lesion on the left temporal lobe at subcortical level. Brain MRI (fig 1A) evidenced a haemorrhagic lesion involving the left putamen and the external capsule near the insula. The lesion was located next to the acoustic radiation (fig 1 A and B). Cerebral angiography was normal. Three EEG recordings (performed on days 1, 3, and 5 after admission) highlighted only a mild abnormal slow activity at the temporal level, without epileptiform grapho-elements. Audiograms and brain stem auditory evoked potentials were normal.

Transient musical hallucinosis has been described in several situations, such as psychiatric disorders, alcoholism, drug and chemical intoxication, ear and acoustic nerve diseases and, rarely, brain stem lesions mainly involving the tegmentum. Even if musical hallucinosis has been reported in hemispheric lesions a clear relation with the central acoustic pathway has never been described.

In our patient the prolonged duration of the episode, the preservation of consciousness and memory, and the absence of epileptiform abnormalities on EEG rule out an epileptic genesis of musical hallucinosis. In patients with sensory-neural deafness musical hallucinosis may be determined by an increased cortical excitability due to a deafferentation phenomena or by a spontaneous activation of cerebral areas involved in musical perception.

In the present case, it might be directly related to the impairment of the acoustic radiation, containing both ascending (excitatory) and descending (inhibitory) fibres. The
Cochlear implantation in a profoundly deaf patient with MELAS syndrome

Cochlear implantation is now an established technology for restoring hearing in profoundly deaf patients. Adults who have lost all useful hearing in both ears are suitable for cochlear implantation if they are profoundly deaf, (implies hearing thresholds of 100 dB NHL or worse, across the frequency range 125 to 8000 Hz), with aided hearing thresholds worse than 60 dB HL for the frequencies 250 to 4000 Hz and scoring less than 30% in a test of sentence discrimination, using their hearing aids and without lip reading. We describe a patient with MELAS syndrome (mitochondrial myopathy, encephalopathy, lactic acidosis and stroke-like episodes) who became profoundly deaf and who has successfully undergone cochlear implantation and rehabilitation.

A right-handed secretary with MELAS syndrome, and a confirmed A to G mutation at nucleotide 3243 in the mitochondrial genome, was referred to the cochlear implant programme of The Royal National Throat, Nose, and Ear Hospital. She had insulin dependent diabetes, congenital cataracts, short stature, weakness, fatigue, and hearing loss. She had never had encephalopathy or strokes. Her mother is also diabetic, has glaucoma, and has a lesser degree of deafness, and her sister has been profoundly deaf from birth. Her own voice quality had relied greatly on finger spelling and written communication with her family has improved. Her ability to communicate with her family was severely restricted due to profound deafness. As she had virtually no hearing in either ear at 100 dB nHL, her own voice quality had relied greatly on finger spelling and written information. Her own voice quality had relied greatly on finger spelling and written communication with her family has improved.

The patient had begun to experience bilateral hearing loss at the age of 22, with slow deterioration up to the age of 29, by which time she was profoundly deaf in the right ear. By the age of 30 she was also profoundly deaf in the left ear and had developed tinnitus. She had no spontaneous vertigo, but sudden movements could leave her temporarily unsteady. At the age of 30 she was also profoundly deaf in the left ear and had developed tinnitus. She had no spontaneous vertigo, but sudden movements could leave her temporarily unsteady. At the age of 30 she was also profoundly deaf in the left ear and had developed tinnitus. She had no spontaneous vertigo, but sudden movements could leave her temporarily unsteady. At the age of 30 she was also profoundly deaf in the left ear and had developed tinnitus. She had no spontaneous vertigo, but sudden movements could leave her temporarily unsteady.

Imaging studies using both CT and MRI showed mild temporal lobe atrophy at necropsy with associated spongy degeneration of the brain. We describe a patient who died after having deafness, which progressed over 8 years to profound deafness. Her selection as a candidate for cochlear implantation was straightforward, and she has been successful in adapting to the device and has gained a significant benefit from it. The performance of the patient in the BKB word test places her in the top 5% of adult performers in our patient series. Another patient with profound deafness and MELAS, who had had seizures and strokes, has recently been reported incidentally in a large series to have become implanted with a successful outcome, but unfortunately details were not provided.

The fact that this patient has gained considerable benefit from her cochlear implant raises the possibility that other patients with MELAS syndrome and profound sensorineural deafness could benefit from this procedure.
case has been blamed on homeopathic plum lumbermetallicum that the patient used in an attempt to improve the symptoms of multiple sclerosis. The original article states that he used a homemade remedy; this is very unlikely to have been prepared using the strict regime applied by homeopathic laboratories. A correctly prepared remedy would only contain minute traces of lead, not enough to cause toxicity. We consider it worrying when doctors who practice modern science to find answers to often difficult questions will, when it suits, simply make assumptions without appropriate testing of the hypothesis in question.

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Anti-GQ1b IgG antibody syndrome without ophthalmoplegia: clinical and immunological features

I read with interest the review by Odaka et al. of the range of clinical disorders manifesting in patients raised anti-GQ1b IgG antibodies. Their patients were classified into Miller Fisher syndrome, Bickerstaff’s brain stem encephalitis, acute ophthalmoplegic polyneuropathy without ataxia, Guillain-Barré syndrome, and “unclassified”. The last group included patients who all had external ophthalmoplegia and normal tendon reflexes, and also varying degrees of limb, facial, and bulbar weakness. I have recently encountered a patient who developed an acute, sensory polyneuropathy in association with raised anti-GQ1b IgG antibodies, whose clinical features differ from the 194 patients described in their series.

A previously well 35 year old man had an episode of sore throat and dry cough, with associated myalgia and fever, in May 2000. Two weeks later, he developed tingling paraesthesia first in his feet, spreading up to his knees, and then in both hands. He found it difficult to distinguish where the ground was beneath his feet because of reduced sensation. One week into this illness, he developed partial drooping of his right eyelid. He had no symptoms of weakness or double vision. On examination 3 days later, he had a partial right ptosis, but eye movements were normal and he did not report diplopia. Muscle power and tendon reflexes were normal in all four limbs. He had a rather delicate gait because of very mild sensory ataxia with reduced sensation to pain, light touch, and vibration sensation in both legs, to the level of the knees. Joint position sense was impaired in the toes but normal in the fingers.

Nerve conduction studies 3 weeks into his neurological illness showed normal distal motor latencies, proximal conduction velocities, and F wave latencies in all four limbs. All sensory nerve action potentials were absent. Protein in CSF was raised at 0.7 g/l (acellular sample). Chickie & Ig antibodies were raised at 1:64. Antiganglioside antibodies assays showed raised IgG titres to QG1b (1:800), GD1b (1:11000), and GT1b (1:2200). Over the course of the next 2 weeks he improved without treatment, achieving full recovery with no residual symptoms or signs.

The lack of external ophthalmoplegia and ataxia was only encountered in patients classified as Guillain-Barré syndrome in the series by Odaka et al., all of whom had limb weakness and reduced or absent reflexes. The electrophysiologic findings in this patient were not compatible with criteria for demyelinating or axonal Guillain-Barré syndrome, but repeated studies can rarely be normal.1 Electrophysiological studies on patients with Guillain-Barré syndrome, Miller Fisher syndrome, ophthalmoplegic polyneuropathy and positive anti-GQ1b antibody titres have shown marked attenuation or absence of sensory nerve action potentials, suggesting that anti-GQ1b antibodies may be particularly involved in sensory nerve conduction failure.2

A recent report of eight cases of sensory Guillain-Barré syndrome has highlighted the existence of this variant.3 Two of these patients had normal motor nerve conduction studies, one of whom had essentially normal tendon reflexes. Not all of these patients were tested for antiganglioside antibodies.

The QG1b ganglioside is present in both sensory and motor nerves, including oculomotor nerves,1,4 and “unclassified”. The last group included patients who all had external ophthalmoplegia and normal tendon reflexes, and also varying degrees of limb, facial, and bulbar weakness. I have recently encountered a patient who developed an acute, sensory polyneuropathy in association with raised anti-GQ1b IgG antibodies, whose clinical features differ from the 194 patients described in their series.

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Odaka and Yuki reply: Maddison considered that clinical features of his patient were similar to those of “sensory Guillain-Barré syndrome”, as proposed by Oh et al. All of the patients of Oh et al had electrophysiological evidence of demyelination in at least two sensory nerves. By contrast, no evidence of demyelination in sensory nerves was shown in his patient. To produce this evidence, Maddison should have repeatedly performed sensory nerve conduction studies during the convalescent phase. Because sensory nerve action potentials were absent in his patient, the “syndrome of acute sensory neuropathy” as proposed by Windelen et al may be the diagnosis. Only after reporting on a patient with a relapsing form of the acute sensory neuropathy syndrome had the patient rapidly developed marked sensory ataxia without ophthalmoplegia and limb weakness after an upper respiratory tract infection. The symptoms reached their maximum in a few days, followed by subsequent improvement over a few weeks. However, unsteadiness remained as a chronic deficit. Stepwise progression of his symptoms occurred over 15 years with 10 similar relapses. Sensory nerve conduction studies showed the absence of action potentials, and sural nerve biopsy showed the marked loss of large myelinated fibres. The patient’s serum had an extremely high titre of an IgM monoclonal antibody directed against b series gangliosides GD2, GD1b, GT1b, and GQ1b. His IgM reacted neither with GD3 nor with GT1a. An absorption study showed that the anti-GQ1b IgM antibody crossed reacted with GD2, GD3, and GT1b. The common sugar structure (NeuAcα2–8 NeuAcα2–3) (GalNAcβ1–4 Galβ) seems to be the binding site of the IgM antibody. Interestingly, serum IgG from the patient of Maddison reacted with GD3, GD1b, GT1b, and GQ1b, although whether his IgG had antibody activity against GD2 and GD3 was not shown. An absorption study would clarify whether his IgG reacted with a disialosyl residue linked to the internal gangliosome to b series gangliosides. An immunohistochemical study showed localisation of GD1b in the neurons of the human dorsal ganglion. GD1b is also localised in the large neurons of the rabbit dorsal root ganglion, and Kusunoki et al succeeded in the development of sensory ataxic neuropathy by sensitisation with GD1b. Autointoantibody to b series gangliosides including GD1b may function in the development of acute sensory ataxic neuropathy in some patients.

Anti-GQ1b IgG antibody from patients with Miller Fisher syndrome cross reacts with GT1a. GT1a has a disialosyl residue linked to the external gangliosome common to GQ1b, and thus may be the binding site of the IgG antibody. We investigated the fine specificity of anti-GQ1b IgG antibody in serum samples from 82 patients: 56 with Miller Fisher syndrome, 11 with Guillain-Barré syndrome, 13 with Bickerstaff’s brain stem encephalitis, and two with acute ophthalmoplegic external ophthalmoplegia. External ophthalmoplegia was present in all of these patients. Anti-GQ1b IgG antibodies were absorbed by GT1a in 80 (96%) of the 82 samples, by GD2 in 75 (92%), and by the other b series gangliosides GD3, GD2, or GT1b in 24 (29%). The most frequent pattern of fine specificity was the cross reaction with GT1a alone, seen in 56 (68%) samples. By contrast, we recently noted that some patients with the “atatic form of Guillian-Barré syndrome” showed no or minimal external ophthalmoplegia but had anti-GQ1b IgG antibody. Anti-GQ1b IgG antibody from the patients, as well as from patients with Miller Fisher syndrome, were absorbed by GT1a. The finding that atactic Guillian-Barré syndrome and Miller Fisher syndrome have in common an autoantibody with the same fine specificity suggests a continuous range. We should not have used
the term “anti-GQ1b IgG antibody syn- 
drome”, but rather, “anti-GQ1b/GT1a IgG antibody syndrome”, which includes Miller Fisher syndrome, Guillain-Barré syndrome with ophthalmoplegia, Bickerstaff’s brain stem encephalitis, acute ophthalmoparesis without ataxia, and the ataxic form of 
Guillain-Barré syndrome. Maddison did not show that his patient’s IgG had antibody activity against GT1a, but his case could be categorized as the syndrome of acute sensory neuropathy if the patient’s IgG did not react with GT1a. 

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BOOK REVIEWS


This book is written in three parts for medical professionals requiring an introduction to critical appraisal of medical information. The first examines the “justification and validity of medical information”, providing “def-

initions and relevant topics of statistics and epi-
demiology”. The second is devoted to “com-
plementary aspects of systematic critical 
appraisal of medical information”. The third part presents statistical techniques that are commonly used in published ar-
ticles.

It would have been helpful if the reader had been provided with references for the topics discussed and those not pursued. The list of books and published papers given near the end of the book are never referred to in the text. Whereas the Normal and binomial distributions are discussed, no other distributions are covered, in particular the Poisson distribution.

Some readers may find the first few chapters heavy going, but they are worth persevering with. The author should have said that the use of the correlation coefficient for indicating agreement between one test and a gold standard is misleading (see Bland JM

Corrections were made in the image text.
Sustained downgaze in coma after cardiac arrest

K JOHKURA, A KOMIYAMA and Y KUROIWA

J Neurol Neurosurg Psychiatry 2001 71: 278-279
doi: 10.1136/jnnp.71.2.278

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