symptoms after yellow fever, diphtheria, meningococcus, oral polio, BCG, hepatitis A, hepatitis B, cholera, or rubella vaccine.

This audit of patients with GBS and CIDP who have received vaccines suggests that the risk of relapse following immunisation is low. The response rate to the questionnaire was small as a proportion of the membership of the GBS Support Group. This is partly because an unknown but large proportion of members are relatives or friends and not former GBS or CIDP patients.

Only 11 of 311 patients with GBS (3.5%, 95% CL 1.8%, 6.2%) who had been immunised after having the disease reported a recurrence of symptoms. All of the vaccines that were associated with neurological symptom recurrence had also been received by many more patients who remained well. Some of the patients who reported symptoms after receiving vaccines had also received the same or other vaccines on other occasions without experiencing any problems. Only one respondent experienced symptoms that increased their modified Rankin scale score. The risk of relapse severe enough to alter the modified Rankin scale score is 0.3% (95% CL 0.01%, 1.78%) while the risk of a relapse requiring treatment or hospitalisation is at most 1.18% (95% CL).

It is more difficult to draw conclusions about the risk of immunisation for relapse in CIDP because our sample size was smaller. Five (7.7%, 95% CL 2.5%, 17.0%) of 65 patients noted a return of symptoms following immunisation. The reports of minor symptoms or acceleration of deterioration following influenza and pneumococcus vaccines merit caution in recommending these immunisations in patients with CIDP, although the risk of infection in immunosuppressed patients may outweigh any potential risk. Of greatest concern is the risk of relapse following tetanus toxoid, which was 8.7% (95% CL 1.7%, 28.0%) in our patient sample. In view of these figures and previous reports of relapse of CIDP following tetanus toxoid[2 5] patients may wish to avoid routine tetanus toxoid immunisation.

Finally, it is important to acknowledge the difficulties in drawing conclusions from a questionnaire in which the patients reported their diagnostic classification and relapses. It is intuitively likely that more patients who experienced symptoms following immunisation responded to the questionnaire, which would overestimate the frequency of relapses. Consequently the true risks of relapse following immunisations after GBS or in CIDP may be less than those discovered in this audit.

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Hypoglycaemia induced by phenytoin treatment for partial status epilepticus

A 22 year old woman was admitted at our epilepsy unit in status epilepticus. On examination, seizures were characterised by a confusional state with little response to external stimuli, and recurrent, brief, tonic motor manifestations lateralised to the left side. Family history was negative for epilepsy and metabolic disorders. Full term birth was uncomplicated and first psychomotor developmental milestones were normal. In the past medical history there was no sign of any metabolic diseases. There were no reports of cognitive dysfunction or personality disturbances. At the age of 16, the patient presented with epilepsy, which was characterised by two types of seizures: global tonic seizures, which occurred yearly, and brief episodes of loss of contact without any other manifestations, which were rare. The patient was treated for many years with 20 mg of clobazam twice daily. The awake EEGs that were performed routinely during the years of treatment with clobazam showed normal background rhythm with rare epileptiform discharges, characterised by irregular 2–3 Hz spike and wave complexes and localised over both frontal-central regions. Magnetic resonance imaging of the brain, which was performed at the age of 18 years, showed no abnormalities.

On the day of admission at the epilepsy unit, the patient had an urgent EEG that revealed continuous, rhythmic spikes or spike and wave complexes over both frontal-central regions with right predominance. Emergency drug treatment with intravenous lorazepam 4 mg was performed twice with a 15 minute interval, but there was no change in the clinical status. Therefore, after 30 minutes, intravenous phenytoin 1000 mg was given by infusion over a period of 20 minutes, and then an infusion of 750 mg of phenytoin was set up for a period of 24 hours. Clinical symptoms and EEG abnormalities rapidly improved and completely resolved after 40 minutes from the start of the administration of phenytoin.

Nine hours later, while the medical observation was still ongoing, the patient developed an episode of clouding of consciousness, which was preceded by prodromal symptoms, including tachycardia, sweating, light headedness, and irritability. On examination, there was reduction of alertness, confusion, and tachycardia. Pupils were of intermediate diameter and reactive to the light. No focal neurological signs were observed. EEG monitoring did not show any abnormalities. Emergency blood tests revealed severe hypoglycaemia (<20 mg/dl). Prompt correction of the hypoglycaemia was obtained by the intravenous infusion of 50 ml of 50% glucose, and a consequent recovery of consciousness occurred. Phenytoin infusion was then withdrawn and oxcarbamazepine was titrated. In the following days no further episodes of hypoglycaemia were noticed. The patient was therefore investigated with the oral glucose tolerance test, which showed normal levels of plasma glucose, immunoreactive insulin, and immunoreactive insulin/plasma glucose, and with an abdominal CT scan, which did not show evidence of pancreatic insulinoma.

Comment

We have described a patient who experienced a severe episode of hypoglycaemia induced by intravenous phenytoin, which was administrated at the doses recommended for the treatment of status epilepticus.[1] It is known that phenytoin interferes with carbohydrate metabolism.[2] Indeed, it may inhibit the release of glucose stimulated insulin and induce a consequent hyperglycaemia. The ability of phenytoin to inhibit insulin release has been suggested to be related to the blockage of Ca2+ uptake via voltage dependent Ca2+ channels.[3] For this hyperglycaemic propriety, phenytoin has been often used in the treatment of hypoglycaemia induced by inoperable insulinomas.[4]

Beside the well known hyperglycaemic effect of phenytoin, it has been reported that high doses of the drug can induce hypoglycaemia. In particular, a recent study reported a case of hypoglycaemia secondary to an acute voluntary intoxication with 20 g of phenytoin. The authors suggested that the hypoglycaemic episode might be attributable either to an escape from the inhibitory effects of phenitoin on insulin secretion or an increased sensitivity of the tissues to insulin.[5] The striking finding of our case is that the hypoglycaemia is induced by a therapeutical dose of phenytoin, and, to our knowledge, this is the first case of severe hypoglycaemia during treatment with phenytoin for status epilepticus. In this case we have indeed excluded a different aetiology of the hypoglycaemia. In particular, a possible effect on glycaemia produced by status epilepticus,[6] has been considered not relevant, because the status epilepticus was partial and resolved nine hours before the onset of hypoglycaemia. However, what caused hypoglicaemia when a therapeutical dose of phenytoin was administrated is unclear, and further studies are needed to fully investigate the effects of phenytoin on charboidrate metabolism.

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Table 1 Meta-analysis of α synuclein/non-amyloid β component precursor allele and genotype distributions in patients with sporadic Parkinson's disease (PD) and controls in Japan

	Allele* frequency						Genotype frequency	
Study	–2	–1	0	1	2	3	Allele 1 (+)	Allele 1 (–)
Present study								
PD (n=165)	0.009		0.518	0.255	0.200	0.018	0.358	0.642
Controls (n=155)	0.013		0.406	0.355	0.210	0.016	0.497	0.503
	χ^2=9.93, df=4, p=0.042, pc=0.21						χ^2=6.3, p=0.012, pc=0.072	
Izumi *et al*[3]								
PD (n=200)		0.003	0.408	0.248	0.330	0.013	0.390	0.610
Controls (n=250)	0.004	0.002	0.390	0.320	0.272	0.012	0.496	0.504
	χ^2=8.37, df=5, p=0.14						χ^2=5.05, p=0.025, pc=0.15	
Combined								
PD (n=365)	0.004	0.001	0.458	0.251	0.271	0.015	0.375	0.625
Controls (n=405)	0.007	0.001	0.396	0.333	0.248	0.014	0.496	0.504
	χ^2=13.9, df=5, p=0.017, pc=0.099						χ^2=11.4, p=0.00073, pc=0.0044 OR 0.61, 95%CI 0.45 to 0.81	

*Nomenclature of the alleles according to Xia *et al*.[2] Alleles 1, 2, and 3 correspond to alleles 3, 2, and 1, respectively, of Krüger *et al*.[4] pc (corrected p value) was obtained by multiply the p value by the number of alleles. CI, confidence interval; OR, odds ratio.

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Meta-analysis of α synuclein/ NACP polymorphism in Parkinson's disease in Japan

α Synuclein is a presynaptic protein highly and broadly expressed in the brain but its normal function is unknown.[1] The protein is also termed non-amyloid β component precursor (NACP) because of its localisation in amyloid plaques of Alzheimer's disease.[1] However, subsequent studies failed to confirm α synuclein as a component of the amyloid plaque.[1] α Synuclein/NACP is now known to be a major component of Lewy bodies in Parkinson's disease (PD).[1] Point mutations of the α synuclein gene found in three independent PD families suggest that α synuclein may participate in the aetiology of sporadic PD.[1] To address this possibility, several groups reported case-control studies using a dinucleotide repeat polymorphism in the promoter region of the gene.[2] The previous Japanese study by Izumi *et al*[3] found a tendency of a lower frequency of allele 1 in Japanese PD patients than in controls.[3] To examine the trend of association, we performed a similar analysis in 165 PD patients and 155 healthy controls in Japan.

The patients with sporadic PD (97 women and 68 men, mean (SD) age 64 (9.6) years, mean age at onset 56 (11) years) had been under treatment at the neurological clinic of Utano National Hospital. The control group was matched for age (mean 63.0 (8.6) years), sex ratio (97 women and 58 men), and birth place (Kyoto and Osaka prefectures) with the PD patients. The controls were selected from the annual health examination at a city clinic. All participants were Japanese. The institutional ethics committees approved the study protocol and informed consent was obtained from each participant. The dinucleotide repeat polymorphism was analysed as reported.[4] We identified five polymerase chain reaction products with different lengths and termed them according to Xia *et al*[2] as follows: 253 bp, allele –2; 257 bp, allele 0; 259 bp, allele 1, 261 bp, allele 2; and 263 bp, allele 3. Statistical analysis was performed by χ^2 test. The corrected p value (pc) was obtained by multiplying the p value by the number of alleles.

As table 1 shows, in our study allele 1 tended to be less frequent in patients with PD than in controls ($p = 0.042$ for allele distribution and $p = 0.012$ for genotype distribution), although the difference was insignificant after correction by the number of alleles ($pc = 0.21$ for allele distribution and $pc = 0.072$ for genotype distribution). This result was similar to the previous Japanese work.[3] To increase the power of the Japanese PD control analysis, we combined our data with those of Izumi *et al*. (table 1). The meta-analysis showed a significantly lower frequency of the allele 1 positive genotype in patients with PD than in controls even after correction ($pc = 0.0044$, odds ratio 0.61, 95%CI 0.45 to 0.81). These results suggest a negative association of allele 1 with PD in Japanese.

As reviewed by Farrer *et al*,[5] results of studies of white populations have varied—some suggested a significant difference between patients with PD and controls and others did not. We did not combine Japanese data with data from white populations because of the difference in allele distribution between them: the frequencies of alleles 0, 1, and 2 in Japanese are 40%, 33%, and 25%, respectively (table 1), while the frequencies of alleles 0, 1, and 2 range from 22–32%, 58–72%, and 3–9%, respectively, in white studies.[5]

The relation between dinucleotide repeat polymorphism and the functional aspects of α synuclein remains unknown. Lee *et al*[6] recently reported that overexpression of α synuclein in human neuroblastoma cell line retards cell death induced by serum withdrawal or hydrogen peroxide. This suggests that the dose of α synuclein may influence neuronal viability. Thus, in Japanese, allele 1 may be associated with high expression or low degradation of α synuclein.

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