neural hyperactivity. The high frequency discharges in our patient with neuromyotonia consisted of motor unit potential-like waveforms, which did not arise spontaneously, but the high frequency of about 200 Hz clearly showed their ectopic origin.

We think that actual definitions of neuromyotonic discharges emphasising their spontaneous occurrence or initiation by needle movement should be reconsidered and modified.

The presence of VGKC antibodies and clinical, immunological, and electrophysiological response to IVIg treatment are in favour of the role of VGKC blockade in the generation of "evoked" neuromuscular discharges. Antibodies to VGKC found in our patient may have accessed the paranodal region (due to myelin disturbance in polyneuropathy) and blocked fast K⁺ channels similarly to 4-aminopyridine.^{4,5} This would enhance supernormality and could thereby allow a single action potential to trigger another discharge or a train to discharge.

J BEDNARIK
Z KADANKA

Department of Neurology, Faculty Hospital and
Masaryk University Brno, Jihlavská 20, 639 00 Brno,
The Czech Republic

Correspondence to: J Bednarik
jbednar@fnbrno.cz

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Zeta class glutathione transferase polymorphisms and Parkinson's disease

Glutathione transferase genes (*GST*) are candidate genes for Parkinson's disease because they are involved with the metabolism of pesticides, dopamine, and glutathione. Recent reports have suggested an association between Parkinson's disease and polymorphisms of *GSTP1*¹ or *GSTM1* and *GSTT1*.²

Recently we discovered a new polymorphic site in the zeta class G→T (*GSTZ1*) gene.³ This consists of a C6T transition at nucleotide 245 in exon 5 that results in an amino acid change at position 82 from methionine to threonine. The T substitution occurs in 14% of white people. We have previously reported two other polymorphic sites at nucleotides 94 and 124 in exon 3.⁴ There are now thought to be four alleles of *GSTZ1*:

Z1*A (A₉₄A₁₂₄C₂₄₅), *Z1*B* (A₉₄G₁₂₄C₂₄₅), *Z1*C* (G₉₄G₁₂₄C₂₄₅), and *Z1*D* (G₉₄G₁₂₄T₂₄₅). Here we investigated the association of Parkinson's disease, pesticide exposure, and these *GSTZ1* polymorphisms.

DNA was extracted from blood samples collected from patients with Parkinson's disease and matched controls as described previously.¹ This study was approved by the Princess Alexandra Hospital ethics committee. Polymorphisms at nucleotide 94 and 124 were detected by polymerase chain reaction/RFLP analysis as described previously.⁴ To detect the nucleotide 245 polymorphism, PCR was performed with the following primers: 5'AAGAGGTGTAGTGATGGTGC3' and 5'GGTGCAAGTGTAC AAGTGCC3'. The PCR was carried out in a 20 µl reaction volume containing reaction buffer IV (Advanced Biotechnologies, Epsom UK; 20 mM (NH₄)₂SO₄, 75 mM Tris/HCl pH 9.0, 0.1% Tween 20), dNTPs (0.2 mM), MgCl₂ (1.5 mM), primers (0.3 µM each), thermostable DNA polymerase (Advanced Biotechnologies, 0.5 U), and DNA (25 ng). No DNA was added to control reactions. Thermal cycling was carried out using a Corbett capillary thermal cycler under the following conditions: initial denaturation at 94°C for 2 minutes; subsequently 35 cycles of 94°C for 20 seconds, 60°C for 20 seconds, 72°C for 30 seconds; and a final extension of 72°C for 2 minutes. Products of PCR were digested overnight with restriction enzyme *Bsh* 1236I (MBI fermentas) at 37°C and fragments were separated by 8% polyacrylamide gel electrophoresis and stained with ethidium bromide. The restriction enzyme *Bsh* 1236I cleaves the C245 fragment generating 12, 108, and 142 bp fragments and the T245 fragment generating 108 and 154 bp fragments.

We tested 307 Parkinson's disease and 105 control samples. The population samples were in Hardy-Weinberg equilibrium. There were no associations between the nucleotide 245, 94, or 124 polymorphisms and Parkinson's disease (table). A total of 87 patients and 53 controls reported a history of regular pesticide exposure. In this group there was a weak association between the nucleotide 245 genotype and Parkinson's disease (p=0.05) (table). Furthermore, in this group, the *Z1*C* genotype (G₉₄G₁₂₄C₂₄₅) was less common in the patients with Parkinson's disease than in the controls (39% v 52%, OR=0.58, 95% confidence interval (95%CI) 0.36-0.95, p=0.03, not corrected for multiple comparisons).

There was no overall association between the *GSTZ* polymorphisms and Parkinson's disease. However, we found a difference when only those who reported pesticide exposure were analysed. We also combined the data for the three polymorphic sites to determine the frequency of the four *GSTZ1* alleles. The *Z1*C* allele is the most common variant in white control populations.

We found that this allele was less common in patients with Parkinson's disease than controls when stratified for pesticide exposure.

Studies of this nature have limitations related to selection bias, case ascertainment, recall bias, difficulty in assessing extent of exposure, and multiple comparisons. Accordingly, our conclusion that there is a potential association between *GSTZ*, pesticide exposure, and Parkinson's disease must be considered preliminary. Nevertheless, it is interesting that there have now been several reports suggesting an association between the risk of Parkinson's disease, polymorphic variability in detoxification genes, and exposure to environmental toxins. These include CYP2D6 and solvent exposure,⁵ *GSTP* and pesticide exposure⁶ and CYP2D6, pesticide exposure, and Parkinson's disease with dementia.⁶ Thus, it has been recognised that studies examining the association of polymorphic variation in xenobiotic metabolism genes and Parkinson's disease should take into account the effect of exposure to toxins.⁷

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M C TAYLOR
P G BOARD

A C BLACKBURN
John Curtin School of Medical Research, Australian
National University, ACT 2601, Australia

G D MELLICK
Department of Medicine, University of Queensland,
Australia

D G LE COUTEUR
Canberra Clinical School, University of Sydney,
Australia

Correspondence to:
Professor P G Board

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A case of stiff limb syndrome responsive to plasma exchange

Stiff limb syndrome is a recently described, rare condition that is characterised by rigidity within the limbs that progresses in a relapsing and remitting fashion, often with involvement of the sphincters and brain stem.^{1,2} The axial muscles are spared in the early stages of the illness, which helps distinguish it from stiff man syndrome, although it may still represent a similar pathogenic mechanism to that

Association between the frequency of *GSTZ1* polymorphisms and Parkinson's disease

Polymorphism	Controls (n=105)			Patients (n=307)		
	TT	CT	CC	TT	CT	CC
245 C→T	0.04	0.33	0.63	0.02	0.35	0.64
*245 C→T	0.04	0.25	0.72	0.01	0.44	0.55
	AA	AG	GG	AA	AG	GG
94G→A	0.08	0.40	0.52	0.11	0.45	0.44
124G→A	0	0.12	0.88	0.01	0.15	0.84

*Analysis restricted to subjects with a history of regular pesticide exposure (p=0.05).

proposed in stiff man syndrome, in which anti-GAD antibodies are typically seen in about 60% of patients.³ However, patients with stiff limb syndrome seem to have different neurophysiological abnormalities from stiff man syndrome² and fewer of these patients have anti-GAD antibodies; they also typically show a poorly sustained response to baclofen and diazepam. The response to immunotherapy in stiff limb syndrome is not known, whereas patients with stiff man syndrome may respond to intravenous immunoglobulin^{4,5} as well as possibly plasma exchange.⁶⁻⁸ We now report on a patient with stiff limb syndrome who responded dramatically to plasma exchange and in whom an anti-axonal antibody was isolated, suggesting that this condition may have an immunological basis.

A 50 year old retired auxiliary nurse presented with a 10 year history of progressive pain, stiffness, and flexion contractures in her hands, followed by increasing immobility. Her neurological problems began at 24 years of age when she developed viral meningitis based on a headache, fever, and a CSF lymphocytosis, that resolved after a week. At the age of 28 she complained of back and leg pain with urinary retention but displayed no abnormal neurological signs and had a myelogram that was normal. Her leg symptoms resolved, but she continued to complain of urinary retention and frequency, for which no cause was found. She went on to have a urethrotomy which did not relieve her symptoms. At the age of 40 she started to develop stiffness and pain in the hands, which slowly clawed, after which her arms and neck became progressively stiffer and her trunk became increasingly stooped on walking, with additional difficulty raising her arms above her head. Five years after the onset of her symptoms she was incapacitated, required assistance with all activities of daily living, and was permanently catheterised. At this stage a seronegative polyarthritis was diagnosed and she was treated with hydroxychloroquine, prothiaden, and corticosteroids, all without effect. She subsequently had some spontaneous remission but at the time of her referral to us she could only walk 10 yards with one stick and continued to complain of heaviness, pain, and stiffness in the limbs especially the left arm. In addition she had developed an intermittent tremor of the right arm and leg, which sometimes affected her jaw and she had difficulty swallowing large boluses of food.

Examination at this time showed her to have flexion contractures of all fingers. She had irregular jerking movements of her right arm and leg that were accentuated by moving the limb or walking a few steps. She had difficulty standing up from a chair without assistance and although she was not weak on formal examination, all limb movements were accompanied by pain. No reflex or sensory abnormalities were found and her plantar responses were flexor.

Investigations showed normal nerve conduction studies as well as a normal CSF examination including negative oligoclonal bands; brain and spine MRI, and routine haematological and biochemical tests were also normal. Her autoantibody screen was negative as were her anti-GAD and anti-neuronal antibodies although an anti-axonal antibody was detected in her serum which is currently being further characterised. More extensive neurophysiology showed her to have an abnormal hypersegmented EMG pattern

during muscle spasms although no continuous motor unit activity was recorded at rest. The latency of responses to magnetic stimulation of the motor cortex was normal.

The diagnosis of stiff limb syndrome was made and she was initially treated with diazepam and baclofen, but continued to deteriorate and gradually lost all useful function of her arms. There was a similar lack of response to intravenous methylprednisolone, so she was given intravenous immunoglobulin, to which she developed an anaphylactic reaction. Her disorder progressed and she developed prominent rigidity and spasms of the face, trunk and limbs. Her speech developed a strangled quality and she had episodes of involuntary tachypnoea apparently due to spasm of respiratory muscles. She was bed bound and totally dependent for all activities of daily living, needing constant nursing. As a result it was decided to give her empirical treatment with two courses of plasma exchange in November and December 1996. After the first exchange, the spasms of her facial and respiratory muscles ceased and after the second there was a slow sustained improvement in limb power, so that after 6 months she had regained independence. For the next 18 months she walked and lived normally, even travelling on holiday. This improvement was punctuated by two admissions with chest infections and impaired respiratory function, which responded well to antibiotics.

Unfortunately the stiffness and tremor of her limbs returned in June 1998 and by November of that year, she was once again immobile and dependent such that she could barely wash herself and was unable to walk at all. Any attempt to move her limbs caused disabling tremor and stiffness. Again, reflexes and plantars were normal. She had a further course of plasma exchange and again responded slowly, such that 3 months later she was able to walk on two sticks. This improvement was initially sustained although she has required a further course of plasma exchange in February 2000 and has now been started on oral cyclophosphamide with notable benefit. The patient has not had further neurophysiological investigations.

This case has all the features of stiff limb syndrome with the novel finding of anti-axonal antibodies detected in the serum. The patient failed to respond to baclofen and diazepam and could not tolerate intravenous immunoglobulin but did have a dramatic and sustained response to plasma exchange, although the need for repeated courses of this treatment has led to her being started on cyclophosphamide. This has not been reported before for this condition and whereas this case illustrates the possible therapeutic effect of this treatment, it also raises the possibility that stiff limb syndrome may have an immunological basis.

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A COLES

Department of Neurology, Norfolk and Norwich Health Care NHS Trust, Brunswick Road, Norwich Norfolk NR1 3SR, UK

A COLES

R BARKER

Department of Neurology, Addenbrooke's NHS Trust, Hills Road, Cambridge CB2 2QQ, UK

Correspondence to: Dr R Barker, Cambridge Centre for Brain Repair, Forvie Site, Robinson Way, Cambridge CB2 2PY, UK

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Acute autonomic and sensory neuropathy after interferon α -2b therapy for chronic hepatitis C

Acute autonomic and sensory neuropathy (AASN) is a disorder characterised by acute autonomic and sensory nerve dysfunctions, and well preserved motor nerve function.¹ Although the pathomechanism of AASN is not clear, autonomic and sensory ganglion neuron cell bodies may be the main target of the immune mediated process underlying AASN.² On the other hand, patients treated with interferon may develop neurological complications including neuropathy.³ We report the first case of AASN which can be associated with interferon α -2b therapy for chronic hepatitis C.

A 57 year old Japanese man with chronic hepatitis C had been treated with interferon α -2b since June 1998. On 3 September, a skin eruption abruptly emerged on his chest and rapidly spread over his whole body. There was no history of exposure to toxins and drugs other than the interferon. The interferon therapy was stopped on 7 September; after a total dose of 390 000 000 units. The skin eruption gradually resolved, but 1 week later, numbness appeared in his limbs. Subsequently he became unable to walk and stand. Further, he developed urinary overflow incontinence and bowel distension. He was then transferred to our neurology department on 2 October.

Physical examination disclosed orthostatic hypotension without secondary tachycardia (120/60 mm Hg lying, 85/52 mm Hg sitting, fixed pulse rate 60 bpm) and paralytic ileus. He was catheterised for incontinence. He was drowsy. The pupils were anisocoric although they reacted promptly to light. Other cranial nerves were unremarkable. Muscle strength and bulk were normal. Deep tendon reflexes were generally absent. There were no pathological reflexes. Light touch, pain, and temperature sensations were impaired moderately over the trunk, more so in his limbs. Vibration and joint sensations were impaired severely in the same distribution, and lost in