Table 1 Clinical profiles in patients with Bickerstaff's encephalopathy with or without anti-GQ1b IgG antibody

	Anti-GQ1b IgG			
	Positive		Negative	
Number of patients	15		10	
Sex (M/F)	10/5		7/3	
Median age (range)	52 (17–63)		48 (3–91)	
	n	%	n	%
Antecedent illness:				
Upper respiratory infection	8	53	7	70
Diarrhoea	2	13	0	0
Initial symptoms:				
Diplopia	8	53	5	50
Consciousness disturbance	4	27	2	20
Gait disturbance	3	20	4	40
Blepharoptosis	2	13	0	0
Photophobia	1	7	0	0
Dysesthesia	0	0	2	20
Dysarthria	0	0	1	10
Neurological signs during the course of the illness:				
Consciousness disturbance				
Drowsiness	4	27	9	90
Stupor, semicoma, or coma	3	20	1	10
Blepharoptosis	4	27	4	40
External ophthalmoplegia	15	100	10	100
Internal ophthalmoplegia	6	40	1	10
Nystagmus	8	53	3	30
Facial weakness	5	33	2	20
Bulbar palsy	2	13	2	20
Tendon reflex				
Brisk	7	46	3	30
Normal	1	7	3	30
Decreased	3	20	1	10
Absent	4	27	3	30
Babinski's sign	4	27	3	30
Ataxia	15	100	10	100
Deep sense impairment	0	0	1	10
Superficial sense impairment	1	7	2	20

the treatment for anti-GQ1b IgG antibody syndrome.¹ We think that the treatment should be given for seronegative patients with Fisher syndrome and Bickerstaff's encephalopathy, although we should rule out similar conditions such as Wernicke's encephalopathy, vascular disease involving the brain stem, multiple sclerosis, neuro-Behçet's disease, botulism, myasthenia gravis, brain stem tumour, and pituitary apoplexy, which are listed in table 1 of our article.¹

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Parkin gene related neuronal multisystem disorder

We read with much interest the article on Japanese patients with parkin gene related autosomal recessive juvenile parkinsonism (ARJP) complicated by cerebellar and pyramidal tract dysfunction.¹ Recently, we described a Dutch family with parkin gene related ARJP showing typical levodopa responsive parkinsonism. The proband clinically had additional mild gait ataxia and pathologically showed—besides classic parkin gene related ARJP findings—neuronal loss in parts of the spinocerebellar system—namely, Purkinje cell layer, dentate nucleus, and gracile fascicles.² Just as our Japanese colleagues, we suspected some kind of hereditary multiple system degeneration with predominant parkinsonism until genetic analysis indicated parkin gene related ARJP. Although the non-extrapyramidal abnormalities in the Japanese and in our patients could have been coincidental, the recent Japanese findings seem to confirm that the spinocerebellar and probably also other systems can be affected in parkin gene related ARJP. The fact that the Japanese patients did not respond to levodopa may have very important clinical consequences because it suggests that neurologists have to request an analysis of the parkin gene in

patients with autosomal recessive levodopa non-responsive parkinsonism accompanied by a multisystem disorder.

The authors found identical parkin gene mutations in two unrelated families—namely, deletions extending from exons 3 to 4. Although it is very striking that two unrelated Japanese families showed identical genetic abnormalities, the degeneration of non-extrapyramidal systems is not exclusively related to these particular genetic abnormalities because our compound heterozygous patients showed clearly different mutations—that is, a heterozygous transversion Lys211Asn in exon 6 and a heterozygous deletion of exon 3. Furthermore, as Kuroda *et al*¹ remarked themselves, other patients with similar parkin gene mutations to Kuroda's patients did not show non-extrapyramidal abnormalities, so the genotype-phenotype relation in parkin gene related ARJP remains to be elucidated. However, taken together the findings of Kuroda *et al*¹ and of our own, it seems very probable that the symptoms of parkin gene related ARJP are not necessarily restricted to parkinsonism but can also include signs and symptoms of a neuronal multisystem disorder.

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Authors' reply

Since the first report of autosomal recessive juvenile parkinsonism (ARJP),¹ it has been established as a clinical entity on the basis of age at onset (usually before the age of 40), clinical features and neuropathological findings. The clinical symptoms include homogeneous features such as typical signs of parkinsonism (rigidity, tremor, akinesia), foot dystonia, diurnal fluctuations, sleep benefit, hyperreflexia, a striking response to levodopa, and early susceptibility to levodopa induced dyskinesia.^{2–3} Levodopa responsive parkinsonism is recognised as one of the most important features of ARJP. However, in 1994 we reported on two Japanese patients from a family with autosomal recessive parkinsonism complicated with multiple system degeneration.⁴ The patients exhibited symptoms corresponding to cerebellar and pyramidal tract dysfunctions as well as nigrostriatal dysfunction, and the most prominent feature in the patients was parkinsonism not responsive to levodopa, indicating dysfunction in both nigral dopaminergic neurons and the striatum. The clinical features were sharply contrastive to those in patients with ARJP;

however, an in frame deletion mutation of the parkin gene extending from exons 3 to 4 was unexpectedly detected in our patients. Furthermore, it is notable that the deletion of this region is not specific in the Japanese family and is occasionally found in patients with ARJP in Japan as well as in Europe,³ although parkin mRNA has been analyzed in only a few studies and it is not well known whether large deletions are in frame or out of frame.

We are very interested in the study by van de Warrenburg *et al* showing that the spinocerebellar system was involved in a patient with parkin mutations who exhibited cerebellar ataxia, because ARJP has been neuropathologically characterised by selective degeneration without Lewy bodies in the substantia nigra compacta and locus ceruleus. Their observation is concordant with our assumption that the parkin protein potentially functions not only in the substantia nigra but also in extranigral regions. It seems unlikely that the non-extrapyramidal involvement in ARJP specifically depends on some mutations or deletions of the parkin gene, as Horstink *et al* suggested. Patients with parkin gene mutations, even those in single families, have generally shown a wide range of clinical signs.⁵ These findings suggest that additional factors contribute to the phenotype. Because patients with ARJP have been considered to exhibit homogeneous clinical symptoms, patients with atypical parkinsonism and/or with non-extrapyramidal symptoms have remained to be examined for parkin gene mutations. Further extensive study in these patients will revitalise the insights into pathophysiology of the parkin gene related disorder.

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Obsessive-compulsive phenomenon and Parkinson's disease

Alegret *et al*¹ have systematically studied patients with Parkinson's disease for presence of "obsessive-compulsive traits". This study is based on the evidence that Parkinson's disease and obsessive-compulsive disorder have neuroanatomical overlap in terms of fronto-basal ganglia circuitry involvement. Anatomical specificity of obsessive-compulsive disorder or obsessive-compulsive phenomenon has been previously studied in Tourette's syndrome, Huntington's chorea, Sydenham's chorea etc, but not in Parkinson's disease.² The authors, through a cross sectional design,

found significantly high scores on the Maudsley obsessive-compulsive Inventory (MOCI) and Leyton obsessional inventory (LOI) in severe Parkinson's disease. However, the presentation and interpretation of results merits further elucidation and clarification.

The aim has been mentioned as to "... systematically investigate obsessive-compulsive traits in Parkinson's disease", using MOCI and LOI. Although LOI is used to assess both obsessional symptoms and traits,³ MOCI is used to investigate the different types and rate severity of obsessive-compulsive complaints in patients with obsessive-compulsive disorder.^{3,4} Also, traits are defined as enduring patterns of perceiving, relating to, and thinking about the environment and oneself that are exhibited in a wide range of important social and personal contents⁵ and are part and parcel of the personality of any person. On the other hand, obsessive-compulsive disorder is a clinical disorder characterised by recurrent obsessions or compulsions that causes distress or impairment.⁵ Hence the MOCI is used to assess the obsessive-compulsive symptoms in patients with obsessive-compulsive disorder and is not applicable for obsessive-compulsive traits or neurotic patients with no obsessional symptoms.^{3,4} This issue needs discussion as the authors have interchangeably used the terms "traits", "phenomenon", and "symptoms" leading to considerable semantic confusion. Also, it raises the query as to what is being actually assessed. Are the authors assessing obsessive-compulsive traits or obsessive-compulsive symptoms? To our mind, the attempt has been to assess obsessive-compulsive phenomena (both traits and symptoms); traits using LOI and symptoms using MOCI.

Secondly, it is mentioned that "patients with mild Parkinson's disease had no obsessive-compulsive symptoms". A closer look at the table presented shows that the MOCI total score was 4.83 (SD 3.57) in controls compared with 4.12 (SD 3.15) in patients with mild Parkinson's disease. If such is the case, then the controls demonstrated more (though statistically comparable) obsessive-compulsive symptoms than patients with mild Parkinson's disease. This issue has not been highlighted and discussed. Another related issue is the absence of a cut off score on MOCI that can differentiate between presence or absence of obsessive-compulsive symptoms.^{3,4} Hence, the above statement by the authors is itself not tenable.

Thirdly, it has been suggested that obsessive-compulsive symptoms appeared late during progression of Parkinson's disease (based on correlation between years of evolution and MOCI global score). Keeping in mind the previous issue, this suggestion should be modified to: patients with longer duration of Parkinson's disease had greater severity (rather than emergence) of obsessive-compulsive symptoms. Additionally, a correlation between MOCI total score and stage of Parkinson's disease can just simply be interpreted as: the more progressive the Parkinson's disease, the more prominent/severe is the obsessive-compulsive symptomatology. The assertion that obsessive-compulsive symptoms appeared late during disease progression can only be made if there is a correlation between duration of illness and severity of Parkinson's disease.

Fourthly, the statement "slowness might be expected ... did not increase" is conceptually not tenable as the slowness characteristic of Parkinson's disease can in no way be equated (or compared) with the slowness in obsessive-compulsive disorder (or obsessive-compulsive

slowness); as evidenced from items of slowness and repetition of MOCI.⁴ Also, the obsessive-compulsive slowness is related to obsessions⁵ whereas the slowness in Parkinson's disease has no such cognitive basis.

Lastly, a very interesting and important finding in this study has been that no patient with Parkinson's disease had obsessive-compulsive disorder. Hence, the link between these two may be lacking. But, at the neuroanatomical level, the basic psychopathology seems to be somewhat similar. It may be that a pathoplastic effect is exerted by the frontal and temporal lobes on some basic dysfunction of basal ganglia leading to differing clinical manifestations. This study, indeed, opens up new vistas of research for understanding the neurobiological basis of obsessive-compulsive disorder.

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Authors' reply

We are grateful to Sharma and Gupta for their comments.

(1) We concur with them that the term "phenomena" may be the most appropriate to describe our results because they included measures of traits and symptoms. Patients with Parkinson's disease may show both symptoms and traits. There are several studies suggesting the presence of a characteristic premorbid personality profile in Parkinson's disease. Similarly to obsessive-compulsive disorder, patients with Parkinson's disease demonstrated a previous tendency to inflexibility and mental rigidity.¹ In addition, it has been shown that basal ganglia lesions and induced parkinsonism produce obsessive-compulsive disorder symptomatology.² We think, accordingly, that the use of both MOCI and LOI was pertinent. On the other hand, despite the fact that traits and symptoms can be well differentiated in clinical diagnoses, there is also some evidence supporting a continuum hypothesis.^{3,4}

(2) It is true that the mean of the MOCI scores of patients with mild Parkinson's disease was slightly lower than that of the controls, but without statistical relevance. Thus, we considered it inappropriate to include that issue in the discussion.

(3) Regarding the issue of co-occurrence of severity of Parkinson's disease and obsessive-compulsive disorder phenomena, in addition to the correlation reported in the paper we