SHORT REPORT

Antiganglioside antibody in patients with Guillain-Barré syndrome who show bulbar palsy as an initial symptom

Michiaki Koga, Nobuhiro Yuki, Koichi Hirata

Abstract

***Objectives*—To identify valuable antiganglioside antibodies that support the diagnosis of Guillain-Barré syndrome (GBS) and its variants in patients showing bulbar palsy as an initial symptom.**

***Methods*—Medical records of 602 patients with GBS or its variants were reviewed. Fifteen patients had bulbar palsy as an initial symptom. Serum antibodies against GM1, GM1b, GD1a, GalNAc-GD1a, GT1a, and GQ1b were examined in 13 of them.**

***Results*—Serum antiganglioside antibodies were positive in 11 (85%) patients. IgG anti-GT1a (n=8; 62%) and anti-GM1b (n=7; 54%) antibodies were often present, whereas all the patients had low or no anti-GM1 antibody activity. High anti-GD1a and anti-GQ1b IgG antibody titres were also present in some patients, but most had higher IgG antibody titres to GM1b or GT1a. All five patients with high IgG antibody titre to GM1b or GT1a only had had antecedent diarrhoea. Some patients with pharyngeal-cervical-brachial weakness (PCB) had IgG antibody to GT1a which did not cross react with GQ1b. Other patients with PCB had antibody to GT1a which cross reacted with GQ1b or antibody to GM1b, but anti-GM1b and anti-GT1a antibodies were not associated with the presence of bulbar palsy. All the patients who had no IgG antiganglioside antibodies recovered completely.**

***Conclusions*—Measurement of serum IgG anti-GT1a and anti-GM1b antibodies gives helpful support for the diagnosis of GBS and its variants when there is early involvement of the oropharyngeal function independently of other neurological findings which appear as the illness progresses.**

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Keywords: Guillain-Barré syndrome; bulbar palsy; antiganglioside antibody

Department of Neurology, Dokkyo University School of Medicine, Tochigi, Japan
M Koga
N Yuki
K Hirata

Correspondence to:
Dr Nobuhiro Yuki, Department of Neurology, Dokkyo University School of Medicine, Kitakobayashi 880, Mibu, Shimotsuga, Tochigi 321–0293, Japan.
fax 0081 90 1608 9313;
email: n_yuki@msn.com

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Bulbar palsy may be an initial clinical sign in several neurological or non-neurological disorders.[1] Dysphagia and dysarthria often appear at the beginning of botulism and diphtheria. Myasthenia gravis, brainstem vascular disturbance, multiple sclerosis, and tumour invasion to the vagus nerve sometimes show oropharyngeal dysfunctions early in the clinical course. Guillain-Barré syndrome (GBS) also may have the initial neurological sign of bulbar palsy, although very rarely.[2] Patients with GBS should be treated with plasmapheresis or intravenous immunoglobulin as soon as possible to shorten the duration of disability.[3–6] It is therefore important to differentiate GBS and its variants, which show early oropharyngeal dysfunctions, from other disorders. Physiological studies and CSF testing, however, may detect no abnormalities in some patients with GBS who show bulbar palsy early.[7]

Measurement of serum antiganglioside antibodies should prove useful for supporting the diagnosis of GBS or its variants. The major gangliosides GM1 and GD1a[8–11] and the minor ones GM1b, GalNAc-GD1a, and GT1a[12–17] in bovine brain are target molecules for the autoantibodies found in GBS and its variants. The presence of IgG anti-GM1 antibody, strong supportive evidence for the diagnosis of GBS, however, is not common in patients with GBS with cranial nerve involvement.[18] Furthermore, there are only a few reports on serum antiganglioside antibodies in patients with GBS or its variants who show bulbar palsy as an initial symptom,[17 19–21] and it is not clear which antiganglioside antibodies are useful for differentiating GBS with early oropharyngeal dysfunction from other disorders. To assess the diagnostic value of the antiganglioside antibodies present in patients with GBS and its variants who had bulbar palsy as an initial symptom, we examined the frequencies of detectable serum antibodies to various gangliosides, including minor ones, in these patients and the relation of antiganglioside antibodies to clinical features.

Patients and methods

PATIENTS

Medical records were reviewed of 387 patients with GBS, 156 with Fisher's syndrome (FS), 36 with Bickerstaff's brainstem encephalitis (BBE), and 23 with acute ophthalmoparesis, all

Table 1 Clinical features of patients with GBS with the initial symptom of bulbar palsy

No	*Age/sex*	*Antecedent events*	*Symptoms at onset*	*OP*	*FP*	*Limb weakness*	*Therapy*	*Outcome (time after onset)*
1	33/M	URTI	BP, weakness in legs	-	+	+ (arms=legs)	PP	Severe limb weakness (10 weeks)
2	23/M	Diarrhoea	BP, dysaesthesia	-	+	+ (arms>legs)	PP	Unknown
3	14/M	Diarrhoea	BP	+	+	+ (arms=legs)	PP, others	Moderate arm weakness, mild OP (4 months)
4	34/F	URTI, diarrhoea	BP, dysaesthesia	+	+	-	PP	Mild OP (5 months)
5	37/M	Diarrhoea	BP, blurred vision	+	-	+ (only in arms)	Steroid iv	Mild OP (4 weeks)
6	55/F	URTI, diarrhoea	BP, nausea, ptosis	+	+	+ (arms>legs)	Steroid im	No deficit (3 months)
7	19/M	Absent	BP, OP	+	-	-	PP	Mild OP (3 weeks)
8	33/M	URTI	BP, dysaesthesia	+	+	+ (only in arms)	PP	Mild OP (18 months)
9	29/F	Unknown	BP, dysaesthesia	+	+	-	Not done	Mild OP (4 weeks)
10	44/F	URTI	BP	+	+	+ (arms>legs)	IVIg	Moderate limb weakness (3 months)
11	55/M	URTI, diarrhoea	BP, gait disturbance	-	+	+ (arms=legs)	PP	No deficit (3 months)
12	7/F	Fever	BP	+	+	+ (arms>legs)	IVIg	No deficit (12 months)
13	54/F	URTI	BP, dysaesthesia	-	-	+ (arms>legs)	Not done	No deficit (4 weeks)

URTI=upper respiratory tract infection; BP=bulbar palsy; OP=ophthalmoparesis; FP=facial palsy; PP=plasmapheresis; IVIg=intravenous immunoglobulin.

of whom had been referred to our neuroimmunological laboratory between June 1994 and March 1998 for tests for serum antiganglioside antibodies. Diagnoses of GBS, FS, and acute ophthalmoparesis were based on established clinical criteria.[7 22 23] Patients with BBE fulfilled all the following: (1) presence of external ophthalmoplegia and cerebellar ataxia; (2) consciousness disturbance or presence of long tract signs such as pyramidal signs and hemisensory disturbance; (3) recovery from neurological deficits beginning within 4 weeks of onset; and (4) ability to rule out the diagnosis of cerebral vascular disease, brain tumour, Wernicke's encephalopathy, botulism, multiple sclerosis, or herpes simplex virus encephalitis. Our review of current illness and neurological signs on the day of admission indicated that 15 patients (mean age 34; nine males; six females) had bulbar palsy as an initial symptom (11 patients with GBS, two with FS, one with BBE, and one with acute ophthalmoparesis). Of these 15 patients, serum samples were taken within 4 weeks of the onset of neurological symptoms from 13 (87%) (mean age 34; seven males; six females, table 1), who therefore were included in the present study. The details of patients 5 and 6 have been reported elsewhere.[17 21] To monitor the functional prognosis of the patients, follow up faxes were sent when possible to the physicians who treated the patients during the recovery phase of the illness. Because serum antibodies against GM1b were frequent in patients with GBS with early involvement of the lower cranial nerves, we also examined 175 consecutive patients with GBS (n=124) or FS (n=51) to determine whether the presence of bulbar palsy is significantly related to serum anti-GM1b IgG and IgM antibodies.

ENZYME LINKED IMMUNOSORBENT ASSAY

We measured the serum antibodies to GM1, GM1b, GD1a, GalNAc-GD1a, GT1a, and GQ1b using the enzyme linked immunosorbent assay (ELISA) described elsewhere.[17] Serum was considered positive when the antibody titre was $\geqslant 500$

ABSORPTION STUDY

This study was done as described elsewhere[17] with minor modifications. Antiganglioside antibodies were absorbed in microtitre wells coated with 10 pmole portions of ganglioside. Absorption rates were expressed as percentages of the optical densities obtained with and without absorption treatment.

Results

CLINICAL FEATURES (TABLE 1)

Eleven (92%) of 12 patients for whom clinical data were available had had antecedent symptoms, of which upper respiratory infection was the most frequent (n=7; 58%) and diarrhoea the second (n=6; 50%). The patients often complained of dysaesthesia in the distal extremities at the time bulbar palsy appeared. Facial palsy and ophthalmoplegia were frequent (facial palsy, 77%; ophthalmoparesis, 69%). Muscle weakness was present in some or all limbs in 10 (77%) patients, of whom seven (54%) had arm dominant weakness but no leg dominant weakness. Only one (patient 5), as reported elsewhere,[17] met the clinical criteria for pharyngeal-cervical-brachial weakness (PCB) proposed by Ropper.[2] The other six (patients 2, 6, 8, 10, 12, and 13) with arm dominant weakness also had severe weakness for neck flexion, but did not fulfill the criteria for PCB because areflexia and/or muscle weakness were present throughout the lower limbs. Babinski's sign, drowsiness, ophthalmoparesis, and ataxia were present temporarily in patient 8, in whom the diagnosis of BBE was made. Assisted ventilation was required in five patients (2, 3, 8, 11, and 12). Four patients (6, 11, 12, and 13) made complete recoveries within 3 to 12 months after onset, whereas moderate or severe limb weakness remained in patients 1, 3, and 10 10 weeks to 4 months after onset. Bulbar palsy disappeared in all the patients for whom clinical prognosis data were available. Mild ophthalmoparesis was present in six patients (3, 4, 5, 7, 8, and 9) from 3 weeks to 18 months after onset, but they had no problems in carrying out daily activities.

ANTIGANGLIOSIDE ANTIBODIES

Serum antiganglioside antibodies were positive in 11 (85%) of 13 patients (table 2). IgG anti-GT1a (n=8; 62%) and anti-GM1b (n=7; 54%) antibodies were frequent, whereas anti-GM1 antibody activity was low or not detected. High anti-GD1a and anti-GQ1b IgG antibody titres were found in some patients, but all except one (patient 10) had higher IgG antibody titres to GM1b or GT1a.

Patients were classified into four groups (groups A-D) according to their IgG antiganglioside antibodies (table 2). Group A (patients

Table 2 Antiganglioside antibody titres in GBS patients with the initial symptom of bulbar palsy

	IgG Antibodies to:						*IgM Antibodies to:*					
No	*GM1*	*GM1b*	*GD1a*	*GalNAc-GD1a*	*GT1a*	*GQ1b*	*GM1*	*GM1b*	*GD1a*	*GalNAc-GD1a*	*GT1a*	*GQ1b*
1	500	256000	64000	-	-	-	500	500	-	500	500	-
2	500	128000	1000	-	-	-	-	-	-	500	-	-
3	-	128000	-	500	4000	500	1000	32000	500	32000	-	500
4	-	4000	-	-	500	-	-	1000	-	-	500	-
5	-	-	-	-	32000	-	-	-	-	-	-	-
6	-	1000	-	-	32000	500	-	-	-	-	-	-
7	-	-	-	-	500	-	-	-	-	-	-	-
8	-	4000	64000	-	1024000	256000	-	-	-	-	-	-
9	-	500	-	-	32000	8000	-	1000	-	500	500	500
10	-	-	-	-	2000	8000	-	-	-	-	-	500
11	-	-	-	-	-	-	-	-	-	-	-	-
12	-	-	-	-	-	-	-	-	-	-	-	-
13	-	-	-	-	-	-	-	-	-	-	1000	500

Only titres of ⩾500 are shown.

1–4) had a marked increase in IgG anti-GM1b antibody, which was not absorbed by GT1a or GQ1b, but in some patients were absorbed by GD1a or GM1 (table 3). In group B (patients 5–7), IgG anti-GT1a antibodies that did not cross react with GQ1b were detected as described elsewhere.[17 21] Group C (patients 8–10) had IgG anti-GT1a antibodies which cross reacted with GQ1b and sometimes with GD1a (table 3). Group D (patients 11–13) had no IgG antibodies to the gangliosides used in this study. Thin layer chromatography (TLC) with immunostaining was performed using serum samples from two patients (1 and 8). Serum IgG from patient 1 reacted with GM1b ganglioside but not with others such as GM1, GD1a, GT1a, or GQ1b on TLC (data not shown). The IgG from patient 8 reacted strongly with GT1a and more weakly with GQ1b (data not shown).

Three (75%) of the four patients in group A had had antecedent diarrhoea, and all showed facial palsy. Two had moderate to severe residual muscle weakness 10 to 16 weeks after onset, and one made a complete recovery, except for mild ophthalmoparesis, 5 months after onset. In groups B and C, ophthalmoparesis and arm dominant limb weakness were often present, and minimal residual symptoms of ophthalmoparesis remained. In Group D, ophthalmoparesis was less common and all three patients made a complete recovery. Five (71%) of the seven (patients 2, 5, 6, 8, 10, 12, and 13) with PCB-like symptoms had high IgG antiganglioside antibody titre; two had IgG anti-GT1a antibodies which did not cross react with GQ1b (group B), two had IgG anti-GT1a and GQ1b antibodies which cross reacted with each other (group C), and one had a marked increase in IgG anti-GM1b antibodies (group A).

Table 3 Absorption rate of IgG anti-GM1b antibody and IgG anti-GT1a antibody

Absorber	*GM1*	*GM1b*	*GT1a*	*GD1a*	*GQ1b*
Patient	*Absorption rate of IgG anti-GM1b Ab(%) Absorber*				
1	6	96	2	92	1
2	23	55	0	2	0
3	13	82	0	6	0
4	0	67	0	0	0
Patient	*Absorption rate of IgG anti-GT1a Ab(%) Absorber*				
5	0	0	75	0	0
6	0	0	80	0	0
8	0	4	70	39	59
9	0	0	81	0	37
10	3	14	78	11	98

RELATION OF ANTI-GM1b ANTIBODIES TO BULBAR PALSY

IgG anti-GM1b antibody titres of 500 or more were found in 44 (25%) of the 175 patients with GBS or FS, and IgM antibodies in 21 (12%). Fifty three (30%) of the patients had bulbar palsy. There was no significant association of bulbar palsy with anti-GM1b IgG antibodies (χ^2 test p=0.80; Mann-Whitney *U* test p=0.44) or the IgM (χ^2 test p=0.75; Mann-Whitney *U* test p=0.65).

Discussion

We often found serum antiganglioside antibodies in patients with GBS or its variants in whom bulbar palsy appeared early in the illness. Measurement of these autoantibodies should be useful to distinguish GBS with early involvement of oropharyngeal functions from such other disorders as botulism and myasthenia gravis. Of the antiganglioside antibodies, IgG anti-GT1a and anti-GM1b seem to be particularly valuable as diagnostic markers for GBS and its variants in which there is early appearance of bulbar palsy, because five (38%) of 13 patients (patients 2–6) had very high antibody activity to GT1a or GM1b, and low or no activity to other gangliosides. Conversely, measurement of anti-GM1 and anti-GalNAc-GD1a antibodies does not seem useful for distinguishing GBS from other diseases when bulbar palsy appears early in the clinical course. All five patients (2–6) with high IgG antibody titre only to GM1b or GT1a had had antecedent diarrhoea, whereas patients 1, 8, 9, and 10, with high antibody titres to other gangliosides as well as GM1b and GT1a, often had a history of prior upper respiratory infection. In patients with a history of antecedent diarrhoea in particular, measurement of serum IgG antibodies to gangliosides other than GM1b and GT1a may give false negative results in serological examinations.

GT1a and GM1b are minor human brain gangliosides,[14 24] that also seem to be present on human peripheral nerves.[14 16] The gram negative bacterium *Campylobacter jejuni*, a leading agent of antecedent infection in GBS,[25] was isolated from a stool specimen of one patient (3), who had increased IgG antibody titres against GM1b and GT1a. Some strains of *C jejuni* that had been isolated from patients with GBS have lipopolysaccharides bearing sugars

that mimic those of GT1a[26 27] and GM1b.[15] Molecular mimicry therefore may function in the induction of anti-GT1a and anti-GM1b antibodies which cause neurological deficits such as bulbar palsy in some patients with GBS or its variants, but anti-GT1a[16 17] and anti-GM1b antibodies are not associated with the presence of bulbar palsy in most patients.

Unlike patients with classic ascending GBS, seven (54%) of the 13 patients in this study showed neck and arm dominant muscle weakness, originally described by Ropper in PCB,[2] whereas the tendon reflex was preserved in the legs of only one patient. Although most of the patients with PCB described by Ropper *et al*[7] made slow recoveries, the bulbar palsy in most of the patients in our study completely disappeared. Limb weakness rather than bulbar palsy remained as a residual symptom in some patients who had early bulbar palsy.

Mizoguchi *et al*[19] and ourselves[17 21] reported the detection of IgG anti-GT1a antibody which does not cross react with GQ1b in PCB. We have now confirmed that anti-GT1a antibody which cross reacts with GQ1b and anti-GM1b antibody is also present in some patients with PCB-like symptoms. In three patients with acute oropharyngeal palsy as described by O'Leary *et al*,[20] serum IgG antibodies against GT1a and GQ1b were found during the acute phase of the illness. None of the patients had ophthalmoplegia during the clinical course, even though IgG anti-GQ1b and anti-GT1a antibodies are closely associated with the presence of ophthalmoplegia.[28] In another patient with GBS, described by Mizoguchi *et al*,[29] who had bulbar palsy and generalised muscle weakness but no ophthalmoplegia, the IgG anti-GQ1b and anti-GT1a antibody titres were also raised. We have confirmed that patients who initially had bulbar palsy and later ophthalmoparesis also had raised IgG antibody titres to GQ1b and GT1a as do patients with "typical" FS. We speculate that the involvement of the oculomotor nerves in acute oropharyngeal palsy depends on the severity of the illness and that acute oropharyngeal palsy with increased serum IgG antibody titres to GQ1b and GT1a can be defined as an early clinical stage of FS, BBE, or PCB.

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1 Hughes TAT, Wiles CM. Neurogenic dysphagia: the role of the neurologist. *J Neurol Neurosurg Psychiatry* 1998;**64**:569–72.
2 Ropper AH. Unusual clinical variants and signs in Guillain-Barré syndrome. *Arch Neurol* 1986;**43**:1150–2.
3 Guillain-Barré Syndrome Study Group. Plasmapheresis and acute Guillain-Barré syndrome. *Neurology* 1985;**35**:1096–104.
4 French Cooperative Group on Plasma Exchange in Guillain-Barré Syndrome. Efficiency of plasma exchange in Guillain-Barré syndrome: role of replacement fluids. *Ann Neurol* 1987;**22**:753–61.
5 van der Meché FGA, Schmitz PIM, the Dutch Guillain-Barré Study Group. A randomized trial comparing intravenous immune globulin and plasma exchange in Guillain-Barré syndrome. *N Engl J Med* 1992;**326**:1123–9.
6 Plasma Exchange/Sandoglobulin Guillain-Barré Syndrome Trial Group. Randomised trial of plasma exchange, intravenous immunoglobulin, and combined treatments in Guillain-Barré syndrome. *Lancet* 1997;**349**:225–30.
7 Ropper AH, Wijdicks EFM, Truax BT. *Guillain-Barré syndrome*. Philadelphia: FA Davis, 1991:18–21, 106–21.
8 Yuki N, Yoshino H, Sato S, *et al*. Acute axonal polyneuropathy associated with anti-GM1 antibodies following Campylobacter enteritis. *Neurology* 1990;**40**:1900–2.
9 Yuki N, Yoshino H, Sato S, *et al*. Severe acute axonal form of Guillain-Barré syndrome associated with IgG anti-GD1a antibodies. *Muscle Nerve* 1992;**15**:899–903.
10 Rees JH, Gregson NA, Hughes RAC. Anti-ganglioside GM1 antibodies in Guillain-Barré syndrome and their relationship to Campylobacter jejuni infection. *Ann Neurol* 1995;**38**:809–16.
11 Carpo M, Nobile-Orazio E, Meucci N, *et al*. Anti-GD1a ganglioside antibodies in peripheral motor syndromes. *Ann Neurol* 1996;**39**:539–43.
12 Kusunoki S, Chiba A, Kon K, *et al*. *N*-acetylgalactosaminyl GD1a is a target molecule for serum antibody in Guillain-Barré syndrome. *Ann Neurol* 1994;**35**:570–6.
13 Yuki N, Taki T, Handa S. Antibody to GalNAc-GD1a and GalNAc-GM1b in Guillain-Barré syndrome subsequent to Campylobacter jejuni enteritis. *J Neuroimmunol* 1996;**71**:155–61.
14 Kusunoki S, Iwamori M, Chiba A, *et al*. GM1b is a new member of antigen for serum antibody in Guillain-Barré syndrome. *Neurology* 1996;**47**:237–42.
15 Yuki N, Tagawa Y, Irie F, *et al*. Close association of Guillain-Barré syndrome with antibodies to minor monosialogangliosides GM1b and GM1α. *J Neuroimmunol* 1997;**74**:30–4.
16 Ilyas AA, Cook SD, Mithen FA, *et al*. Antibodies to GT1a ganglioside in patients with Guillain-Barré syndrome. *J Neuroimmunol* 1998;**82**:160–7.
17 Koga M, Yuki N, Ariga T, *et al*. Is IgG anti-GT1a antibody associated with pharyngeal-cervical-brachial weakness or oropharyngeal palsy in Guillain-Barré syndrome? *J Neuroimmunol* 1998;**86**:74–9.
18 Jacobs BC, van Doorn PA, Schmitz PIM, *et al*. Campylobacter jejuni infections and anti-GM1 antibodies in Guillain-Barré syndrome. *Ann Neurol* 1996;**40**:181–7.
19 Mizoguchi K, Hase A, Obi T, *et al*. Two species of antiganglioside antibodies in a patient with a pharyngeal-cervical-brachial variant of Guillain-Barré syndrome. *J Neurol Neurosurg Psychiatry* 1994;**57**:1121–3.
20 O'Leary CP, Veitch J, Durward WF, *et al*. Acute oropharyngeal palsy is associated with antibodies to GQ1b and GT1a gangliosides. *J Neurol Neurosurg Psychiatry* 1996;**61**:649–51.
21 Kashihara K, Shiro Y, Koga M, *et al*. IgG anti-GT1a antibodies which do not cross-react with GQ1b ganglioside in a pharyngeal-cervical-brachial variant of Guillain-Barré syndrome. *J Neurol Neurosurg Psychiatry* 1998:**65**:799.
22 Asbury AK, Cornblath DR. Assessment of current diagnostic criteria for Guillain-Barré syndrome. *Ann Neurol* 1990; **27**(suppl):S21–4.
23 Yuki N. Acute paresis of extraocular muscles associated with IgG anti-GQ1b antibody. *Ann Neurol* 1996;**39**:668–72.
24 Ando S, Yu RK. Isolation and characterization of a novel trisialoganglioside, GT1a, from human brain. *J Biol Chem* 1977;**252**:6247–50.
25 Rees JH, Soudain SE, Gregson NA, *et al*. Campylobacter jejuni infection and Guillain-Barré syndrome. *N Engl J Med* 1995;**333**:1374–9.
26 Aspinall GO, McDonald AG, Pang H, *et al*. Lipopolysaccharides of Campylobacter jejuni serotype O:19: structures of core oligosaccharide regions from the serostrain and two bacterial isolates from patients with Guillain-Barré syndrome. *Biochemistry* 1994;**33**:241–9.
27 Yuki N, Handa S, Tai T, *et al*. Ganglioside-like epitopes of lipopolysaccharides from Campylobacter jejuni (PEN 19) in three isolates from patients with Guillain-Barré syndrome. *J Neurol Sci* 1995;**130**:112–6.
28 Chiba A, Kusunoki S, Obata H, *et al*. Serum anti-GQ1b IgG antibody is associated with ophthalmoplegia in Miller Fisher syndrome and Guillain-Barré syndrome: clinical and immunohistochemical studies. *Neurology* 1993;**43**:1911–7.
29 Mizoguchi K, Uchiyama T, Obi T, *et al*. Anti-GQ1b and anti-GT1a IgG antibodies in a patient with acute demyelinating polyradiculoneuropathy without ophthalmoplegia. *J Neurol Neurosurg Psychiatry* 1997;**63**:410–1.