organic brain syndrome was more likely. By February 1998 it was clear that he had a receptive and expressive dysphasia and right extensor plantar response. Thyroid function, B12 and folate, an autoimmune screen, protein electrophoresis, serum copper, serum caeruloplasmin, heavy metal screen, porphyria screen, IgA antibodies to gliadin, serological tests for *Treponema* and human immunodeficiency virus tests were all normal. Protein in CSF was mildly raised at 0.62 g/l and contained 2 white cells/mm^3. Oligoclonal bands and CSF 14–3–3 protein were negative. Repeat EEG demonstrated a left hemispheric slow wave focus, cranial MRI showed atrophy of the whole of the left hemisphere, and a SPECT perfusion scan demonstrated marked underperfusion of the posterior temporoparietal cortex on the left. A tonsilar biopsy for protease resistant PrP was negative. The open reading frame of the prion protein gene demonstrated no mutations. The codon 129 genotype was valine homozygous.

By October 1998 he was dependent on his wife for dressing, toileting, and feeding. He was mute with eyelid apraxia, generalised myoclonus, marked primitive reflexes with Gegenhalten tone in the limbs, and bilateral extensor plantar responses. In March 1999 he was in a state of akinetic mutism and died in August 1999. Necropsy disclosed cerebral atrophy, and neuropathological studies showed a spongiform encephalopathy which was most marked in the basal ganglia, with widespread neuronal loss and gliosis. No amyloid plaques were identified. Immunocytochemistry showed a positive reaction in a reticular and perineuronal distribution in the cerebral cortex and the cerebellum, but no PrP plaques were present. Immunocytochemistry for PrP on lymphoid tissue in the spleen and appendix was negative. Western blot analysis of frozen cerebral tissue showed a PrP^{RES} type 1 pattern.[3]

Early age of onset, protracted psychiatric prodrome, and duration of illness distinguish variant CJD clinically from sporadic CJD. Two possible explanations arise for the case described. Firstly, the case represents sporadic CJD, of which there have only been two cases younger than 30 in the United Kingdom since 1970.[4] Neuropathological review of these two earlier cases has found changes in the brain consistent with sporadic CJD; full clinical and genetic data are not available on these cases, but neither showed evidence of PrP^{RES} accumulation in lymphoid tissues. The lack of characteristic neuropathology of vCJD in the brain, the absence of detectable PrP in the tonsil appendix and spleen, together with a PrP^{RES} type 1 pattern in the cerebral cortex all provide supportive evidence for this being a case of sporadic CJD, similar to the other rare cases occurring in valine homozygotes with a type 1 PrP^{RES}.[3] A less likely explanation is that this case may represent bovine spongioform encephalopathy (BSE) infection in a valine homozygous person without the characteristic pattern of PrP glycosylation occurring in BSE and related disorders in animals and humans.[5] This case emphasises the importance of detailed clinical, neuropathological, genetic, and biochemical studies in all cases of suspected CJD, particularly in young people with a valine homozygous or heterozygous codon 129 PrP genotype. Further investigation of such cases by strain typing studies may be required to establish their relation to the BSE agent.

We acknowledge Dr MW Head, NCJDSU; Professor J Collinge, MRC Prion Unit and Department of Neurogenetics, Imperial College School of Medicine at St Mary's, London; and Dr RJS Wise, MRC Cyclotron Unit, Imperial College School of Medicine, Du Cane Road, London, UK.

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Multiple sclerosis treatment trial precipitates divorce

We have noted an unusually high rate of divorce among participants in a recent small treatment trial of multiple sclerosis.[1] Of the 29 patients in the study, 19 were married at entry. During the 18 months of follow up, six patients (31%) became involved in divorce proceedings. In four of these, the unaffected spouse left the marriage for another partner. There was a transient breakdown in one other marriage, which did not lead to divorce, after an extramarital affair by the unaffected partner. Since the study ended, there has been one further divorce after an affair by the unaffected spouse. Those patients who became divorced were not distinguishable by their disability, the efficacy of their treatment, or the duration of their disease or marriage.

The divorce rate in this study, equivalent to an annual rate of 21% of married couples, is considerably greater than the annual divorce rate in the United Kingdom for age and sex matched married couples of 2.4%-3.1%.[2] Physical disability due to any cause is a risk factor for divorce[3] and multiple sclerosis is no exception.[4] However, this effect is not sufficient explanation to account for the exceptionally high divorce rate seen during this study. In one Australian study, the most severely disabled patients with multiple sclerosis were four times more likely to have been divorced than the less disabled; but even among the most disabled the prevalence of divorce was only 13%-18% of all prevalent patients.[5] We suggest that participation in a treatment trial indirectly precipitates divorce, by exposing marital dissatisfaction in the unaffected spouse. One possible explanation may be that trial participation focuses attention on the affected spouse's disability. Alternatively, perhaps the frequent attentions of an interested medical team during a trial relieve the unaffected partner of a sense of responsibility towards his or her spouse. Another interpretation might be that recruitment to therapeutic trials is biased towards those patients who perceive a greater degree of dissatisfaction with their personal situation. To the best of our knowledge, in no previous treatment trial in multiple sclerosis, nor indeed of any other disease, has such a high rate of divorce been noted.

In the light of these findings it may be prudent to make patients and their spouses (or partners) aware, during the recruitment interviews for clinical trials, of the strains which participation may expose in their relationship.

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Allodynia: a sensory analogue of motor mirror neurons in a hyperaesthetic patient reporting instantaneous discomfort to another's perceived sudden minor injury?

Parietal injury may affect spatial cognition in at least three ways: right sided damage may cause left inattention (unilateral neglect), whereby the patient ignores or fails to attend to objects or events on the contralateral (left) side of extrapersonal space[1]; in a rare extension of this disorder, the patient may also experience the presence (often fluctuating) of an additional, supernumerary or phantom limb[2]—for example, a further arm at the midline in addition to a normal one on the right, and a paralysed, neglected, or "missing" one on the left. Finally, in the Gerstmann syndrome there may be, after left parietal damage, simultaneously, left-right disorientation, acalculia, agraphia, and problems with finger (or other body part) localisation or identification. Conversely, with amputation or loss (even congenital) of a limb in an otherwise healthy individual, a phantom limb may be experienced,[3] with the vivid hallucinatory experience of the continued presence of that limb; parietal mechanisms have again been invoked.

The parietal cortex interconnects with the ventral premotor cortex which, as area F5 in monkeys, contains neurons that discharge both when an animal grasps or manipulates objects, and when it sees another individual making similar actions.[4] These "mirror neurons" seem to represent a system that matches observed events to similar, internally generated actions, and thus forms a link, as the authors note, between observer and actor.

In humans, areas in the left inferior frontal and right superior parietal cortex become active both when producing and when seeing finger movements in others.[5] Could similar mirror activity arise in a purely sensory context, such that a person, due maybe to inhibitory failure, may experience pain in a finger or limb when seeing sudden trauma (for example, a blow) to a corresponding area in another person? We report the anecdotal account, from a widow, of her late husband's apparent experience of such "mirror pain" or, as we would suggest, "allodynia".

The deceased, a long time smoker, died in late February 1993 with the diagnosis of "extensive metastatic carcinomatosis", antecedent cause, "carcinoma of the right lung". (The widow, however, questions the lung cancer diagnosis, and claims that symptoms of serious rheumatoid disease involving cervical spine and dysphagia were misinterpreted.) As a consequence of increasing pain and stiffness beginning in the neck and upper body, and chest symptoms, he underwent radiography of the cervical spine and chest in August 1990, disclosing opacity in the right lung and slight tracheal deviation; he had increasing difficulty swallowing with food inhalation. Unwillingly, he underwent radiotherapy in early November 1990 to alleviate dysphagia, although according to the widow subsequent gastroscopy indicated that this may have been unnecessary.

He was reported to be very sensitive to touch; even the slightest hand contact gave the impression of sharp fingernails. Of particular interest was his widow's recent observation that "If I slightly knocked my finger, spontaneously showing him, he would immediately grasp his own finger and say "don't do that" (meaning not to show him); He actually felt it. If I merely commented (that I had knocked my finger), there was no such reaction". In interview, she recounted other similar events. The experience was suddenly immediate and intense, and, apparently, qualitatively similar to the hypersensitivity occasioned by actual contact. She had initially contacted one of us (JLB) after hearing a radio broadcast by him of phantom limb phenomena, and wondered whether an analogous mechanism of some kind may have been operating with her late husband.

Although mirror motor neurons may be fundamentally important in learning to act, an adaptive role is far less obvious for perceiving another's pain. Perhaps during infancy avoidance of noxious stimuli is facilitated by early recognition of pain in others. Alternatively the phenomenon may merely be adventitious consequence of disruption of convergent sensory systems. Thus hyperalgesia, where a light touch induces an unpleasant sensation in the same person, is typically attributed to dysfunction of convergent sensory neurons in the neuraxis, though any of several CNS levels may be involved. However where, as here, a separate person is implicated, there may be additional limbic involvement, given the rather intensely emotional aversive aspects of the sensory experience.

Unfortunately no CT or MRI seem to have been performed of the brain, but it is probable that there was fairly widespread CNS involvement. He had also, apparently, experienced head trauma in the war. It would be of interest to know whether similar "allodynia" has been seen after known damage that includes left inferior cortex (opercular region), or the rostralmost region of the right superior parietal lobule.[5] It would also be interesting to get persons, normal or hyperalgesic, to note reactions to noxious stimuli in others while judging the intensity of mildly aversive tactual stimuli they receive themselves.

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Acquired hepatocerebral degeneration: full recovery after liver transplantation

Liver diseases may give rise to variable degrees of neurological impairment, which mostly consist of the syndrome of hepatic encephalopathy, due to the toxic effect of ammonia on the brain during episodes of liver decompensation. In a minority of patients, repeated episodes of liver failure can lead to a chronic progressive encephalopathy, not necessarily related to hyperammonaemia, known as acquired hepatocerebral degeneration (AHD).[1] The pathogenesis of AHD is unclear, but the relation with the acute form of hepatic encephalopathy seems a crucial point. Cerebral deposition of manganese may have a pathogenetic role. The disease may appear after one or more episodes of hepatic coma or, rarely, become manifest in the absence of them. Neuropathology typically discloses degenerative changes in the basal ganglia. The modern techniques of neuroimaging disclose these lesions in vivo.[2] The clinical picture varies, neuropsychiatric changes and movement disorders usually being prominent. The syndrome is poorly responsive to medical therapy, thus being considered largely irreversible.

We report on a patient with AHD who was cured by liver transplantation.

A 59 year old man came to us in November 1997 for a neurological consultation before inclusion in the waiting list for liver transplantation. He had a history of chronic hepatic disease—alcohol and HCV related liver cirrhosis—which had begun some years before. No familial hepatic or neurological diseases were reported. In 1995 he had an episode of hepatic encephalopathy, consisting in somnolence and confusion lasting 36 hours. At the time of examination, the patient had stopped alcohol consumption 1 year before; liver failure was grade C-10 of the Child-Pugh classification. Copper balance was normal. Neurological examinations and EEG gave normal results. The patient was put on the waiting list for liver transplantation. In February and March 1998, he had two episodes of mild ascites with signs of encephalopathy (confusion and asterixis), both reversed by medical therapy. In April 1998 the patient began to complain of sleep disorders, tremor, dysarthria, motor slowness, and subtle cognitive dysfunction, not reversed by medical therapy for hepatic dysfunction. On 6 June 1998, his neurological suitability for liver transplantation was reconsidered. He seemed alert, oriented, and cooperative, with a slight slowness of psychomotor activity. The neurological examination showed hypomimia, dysarthria, bradykinesia, oral dyskinesia, and mild bilateral hand tremor. Neuropsychological examination showed a remarkable impairment of information processing control (attention, vigi-

Neuropsychological testing before and after liver transplantation (LT)

Test	*Cut off*	*Score* before LT*	*Score* after LT (3 months)*	*Score* After LT (12 months)*
Information processing control:				
Attentional matrices (visual search)	31	9	40.2	47.2
Trail making form A: time	93	84	66	27
Trail making form B: time	282	275	168	81
Stroop: word				
Time	38	76	19	15
Errors	2	0	0	0
Colour				
Time	35	58	29	31
Errors	1	4	1	0
Colour/word				
Time	80	124	130	85
Errors	9	10	13	22
Letter A cancellation: errors	9	24	15	5
Digit symbol substitution	19	12	19	18
Auditory reaction times (ms)		281	220	197
Visual reaction times (ms)		423	340	339
Word fluency (F, A, S)	17.3	17.3	26.3	29.3
Raven's coloured matrices (1947)	18.9	19.3	20.3	22.3
Memory:				
Digit span	3.7	4.5	5.5	5.5
Corsi's blocks	3.7	3.7	3.7	3.7
Immediate visual memory	13.8	12.4	16.4	13.4
Rey's 15 words:				
Short term	28.5	37.4	49.4	45.4
Long term	4.7	11.2	12.2	9.2
Paired associate learning	6.5	10	11.5	11
Story recall	4.7	10.6	12.1	4.5
Supraspan spatial learning	5.7	4	14.6	8.7

*Corrected for age and schooling when needed.