The 12 year prognosis of unilateral functional weakness and sensory disturbance

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See Editorial Commentary, p 557

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Background: Although the symptoms of unilateral “medically unexplained” or “functional” weakness and sensory disturbance present commonly to neurologists, little is known about their long term prognosis.

Objective: To determine the long term outcome of functional weakness and sensory disturbance.

Patients: A previously assembled cohort of 60 patients seen as inpatients by consultant neurologists in Edinburgh between 1985 and 1992 and diagnosed as having unilateral functional weakness or sensory disturbance.

Methods: Current symptoms, disability, and distress were assessed by postal questionnaire to the patients and their family doctors.

Results: Follow up data relating to mortality were obtained in 56 patients (93%) and to current diagnosis in 48 patients (80%). Patient questionnaire data were obtained in 42 patients (70%). The median duration of follow up was 12.5 years (range 9 to 16). Thirty five of the 42 patients (83%) still reported weakness or sensory symptoms, and the majority reported limitation of physical function, distress, and multiple other somatic symptoms. Twenty nine per cent had taken medical retirement. An examination of baseline predictors indicated that patients who had sensory symptoms had better functioning at follow up than those who had weakness. Only one patient had developed a neurological disorder which, in hindsight, explained the original presentation. Another patient had died of unrelated causes.

Conclusions: Many patients assessed by neurologists with unilateral functional weakness and sensory symptoms as inpatients remain symptomatic, distressed, and disabled as long as 12 years after the original diagnosis. These symptoms are only rarely explained by the subsequent development of a recognised neurological disorder in the long term.
The questionnaire comprised an initial section inquiring about the presence or absence of 31 somatic symptoms (based on those listed in the DSM-IV diagnostic criteria for somatisation disorder), including weakness and altered sensation. We also asked whether they had stopped working because of ill health. All patients also completed the short form 36 item (SF-36) health status questionnaire—a widely used measure of distress and disability.

We selected two historical control groups with which to compare these results. The first was a sample of 42 patients with multiple sclerosis, surveyed in our department in 1996 and of similar age (median age 41 years) and sex (66% female). The second was from a large study of the local population, undertaken in 1993, from which we extracted median data matched for age and sex.

We also asked the family doctors of all participating subjects (and of patients who had not replied to our letter of invitation) to complete a questionnaire about their patient’s health. The doctors were asked whether their patient had, to their knowledge, developed a neurological disorder. They were also asked to rate the patient’s health, whether they were frequent attenders at the practice, and whether they had a history of medically unexplained symptoms. Replies to each of these three questions were rated on a five point Likert-type scale (strongly agree; agree; neither agree nor disagree; disagree; strongly disagree).

Analysis
We dichotomised the general practitioner ratings according to whether they agreed or disagreed with the three statements about the patient’s health, attendance, and history of medically unexplained symptoms. In an exploratory analysis, we examined differences in outcome according to age (non-parametric linear regression), sex, and whether the symptom was weakness or sensory disturbance (Mann-Whitney test) as predictive variables. The physical functioning and social functioning scales of the SF-36 were used as primary outcome variables.

RESULTS
Completeness of follow up
The recruitment of subjects into the follow up study is shown in fig 1. Of the 60 initial patients, the details of four had been lost in the intervening period. One patient had died (see below) and a further five patients could no longer be traced within south east Scotland. Of the 50 patients for whom we had names and addresses, two refused to take part and six did not reply to the invitation to take part in the study.

Characteristics of patients at follow up
Forty two patients (34 female, eight male) replied to the questionnaire and constitute the follow up sample. The median and mean duration of follow up was 12.5 years (range 9 to 16). The median age at time of initial investigation was 36 years (range 36 to 54 years) (table 1). Thirty one had left sided symptoms and 11 had right sided symptoms. The following investigations had been carried out during the original inpatient assessment of these patients: cerebrospinal fluid analysis (60%), cranial computed tomography (CT) (55%), visual evoked responses (40%), somatosensory evoked potentials (26%), magnetic resonance imaging of the head (21%),

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Table 1 Symptoms at 12.5 year follow up in 42 patients who initially presented with unilateral functional weakness and /or sensory disturbance

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Weakness</td>
<td>69%</td>
</tr>
<tr>
<td>Numbness</td>
<td>48%</td>
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<tr>
<td>Sleep difficulties</td>
<td>67%</td>
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<tr>
<td>Fatigue</td>
<td>58%</td>
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<tr>
<td>Joint pain</td>
<td>57%</td>
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<tr>
<td>Memory or concentration problems</td>
<td>57%</td>
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<tr>
<td>Back pain</td>
<td>55%</td>
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<tr>
<td>Muscle pain</td>
<td>52%</td>
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<tr>
<td>Heavy periods</td>
<td>44%</td>
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<tr>
<td>Depression</td>
<td>43%</td>
</tr>
<tr>
<td>Dizziness</td>
<td>43%</td>
</tr>
<tr>
<td>Headaches</td>
<td>40%</td>
</tr>
<tr>
<td>Gas or bloating</td>
<td>38%</td>
</tr>
<tr>
<td>Nausea</td>
<td>33%</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>33%</td>
</tr>
<tr>
<td>Palpitations</td>
<td>33%</td>
</tr>
<tr>
<td>Breathlessness</td>
<td>31%</td>
</tr>
<tr>
<td>Painful periods</td>
<td>28%</td>
</tr>
<tr>
<td>Sweats</td>
<td>24%</td>
</tr>
<tr>
<td>Anxiety</td>
<td>24%</td>
</tr>
<tr>
<td>Chest pain</td>
<td>21%</td>
</tr>
<tr>
<td>Swallowing difficulties</td>
<td>21%</td>
</tr>
</tbody>
</table>

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*Denominator = 41 (42 patient replies, excluding the patient who was misdiagnosed). *At onset 24 had numbness and 18 had weakness ± numbness. *Denominator = 18 (excluding men, patients with a hysterectomy, and those over 50). *Denominator = 46 (47 family doctor replies excluding the patient who was misdiagnosed).
nerve conduction studies (17%), myelography (12%), and cerebral angiography (10%). Most (62%) had some form of brain neuroimaging.

**Symptom persistence at follow up**
The results in table 1 are derived from the 42 patients who responded to the questionnaire, excluding the one who was misdiagnosed (see below). Overall, 83% of the patients (34/41) reported weakness or numbness as current symptoms, a median of 12.5 years (range 9 to 16) after being initially investigated. Weakness was reported by 69% and numbness by 48%. There was considerable crossover of weakness and sensory symptoms between the time of initial assessment and follow up. Over half (55%) had originally complained of weakness or were found to be weak on initial examination. At follow up, 58% of those who only had sensory symptoms initially went on to develop weakness.

The prevalence at follow up of physical symptoms other than weakness and sensory disturbance was high (table 1). The median number of current symptoms (excluding gynaecological symptoms, depression, and anxiety) was nine. Using DSM-IV criteria and making the assumption that additional reported symptoms were likely to be functional or medically unexplained, six subjects would meet DSM-IV criteria for somatisation disorder (that is, one neurological symptom, four pain symptoms, two gastrointestinal symptoms, and one sexual/gynaecological symptom). Forty one per cent (17/41) had over 10 current physical symptoms.

**Distress and disability at follow up**
The results of the SF-36 health status questionnaire, together with those of the two historical control groups, are shown in table 2. For the 41 patients (n=41, median age 48) symptom data presented in the rest of this paper.

**Prognostic factors**
Patients with only sensory symptoms and signs at presentation had significantly better outcome in terms of higher physical functioning (p < 0.05), social functioning (p = 0.02), and pain (p = 0.01) than patients with any symptoms or signs of weakness (two sided Mann–Whitney test). A higher age of onset predicted lower physical functioning at follow up (p = 0.03, non-parametric linear regression). Sex was not associated with any outcome and no variable predicted medical retirement.

**DISCUSSION**
Functional weakness and sensory symptoms usually persist and remain disabling
After a median of 12 years following initial assessment, 83% of our sample still had weakness or sensory symptoms or both,

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**Table 2 Disability and distress in 41 patients with functional weakness and/or sensory symptoms at follow up compared with multiple sclerosis and local population reference range**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>This study (n=41, median age 48)</th>
<th>MS outpatients in Edinburgh^1 (n=42, median age 41)</th>
<th>Local population reference range^2 (n=1661, median age 47)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical functioning</td>
<td>55 (25 to 80)</td>
<td>20 (0 to 90)</td>
<td>95 (80 to 100)</td>
</tr>
<tr>
<td>Role physical</td>
<td>0 (0 to 56)</td>
<td>25 (0 to 100)</td>
<td>100 (75 to 100)</td>
</tr>
<tr>
<td>Mental health</td>
<td>64 (40 to 76)</td>
<td>68 (4 to 96)</td>
<td>80 (64 to 88)</td>
</tr>
<tr>
<td>Role emotional</td>
<td>33 (0 to 100)</td>
<td>100 (0 to 100)</td>
<td>100 (100 to 100)</td>
</tr>
<tr>
<td>Social functioning</td>
<td>56 (33 to 78)</td>
<td>75 (0 to 100)</td>
<td>100 (60 to 100)</td>
</tr>
<tr>
<td>Energy</td>
<td>30 (15 to 40)</td>
<td>35 (0 to 95)</td>
<td>65 (45 to 75)</td>
</tr>
<tr>
<td>Pain</td>
<td>33 (22 to 67)</td>
<td>92 (0 to 100)</td>
<td>84 (61 to 100)</td>
</tr>
<tr>
<td>General health</td>
<td>40 (20 to 60)</td>
<td>47 (10 to 90)</td>
<td>77 (57 to 87)</td>
</tr>
</tbody>
</table>

All SF-36 scores range from 0 to 100; a lower score equates to poorer health status. SF-36, short form 36-item health questionnaire.
Table 3  Comparison of outcomes and prognostic factors with previous studies of functional motor and sensory symptoms*

<table>
<thead>
<tr>
<th>Year</th>
<th>Sample size</th>
<th>Population sampled</th>
<th>Mean years of follow up</th>
<th>Neurological disorder missed (clinical features)</th>
<th>Disability at follow up</th>
<th>Prognostic factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>1995</td>
<td>56</td>
<td>Neurological inpatients; 73% weakness, 12% gait, 5% sensory only; retrospective</td>
<td>4.5</td>
<td>2 cases (1 bizarre transient weakness due to cerebral ischaemia; 1 ataxia with posturing due to multiple sclerosis)</td>
<td>41% with Rankin scores worse than 2 (“I have symptoms which have caused some changes in my life but I am still able to look after myself”)</td>
<td>Positive: recent onset and recovery by the time of discharge</td>
</tr>
<tr>
<td>1998</td>
<td>64</td>
<td>Neurological inpatients; 50% weakness, 50% movement disorder; retrospective</td>
<td>6</td>
<td>3 cases (all gait disorders, due to (1) myotonic dystrophy, (2) spinocerebellar degeneration, and (3) paroxysmal hemidystonia)</td>
<td>50% had either retired on grounds of ill health or were on sick leave; 36% had a psychiatric disorder</td>
<td>Positive: symptoms present for less than one year; the presence of an axis 1 psychiatric disorder; Negative: receipt of benefits, and litigation</td>
</tr>
<tr>
<td>2000</td>
<td>30</td>
<td>Neurological inpatients; 100% weakness; prospective</td>
<td>1 **</td>
<td>None</td>
<td>43% not working at 1 year</td>
<td>Negative: the presence of a personality disorder, hopelessness, and a concurrent somatic diagnosis</td>
</tr>
<tr>
<td>2000</td>
<td>76†</td>
<td>Psychiatric in- and outpatients; 58% weakness or movement disorder, 37% motor and sensory, 5% sensory</td>
<td>2.4</td>
<td>10 cases (1 weakness due to ALS; 3 movement disorders proven to be organic; 3 gait disorders due to MS, MSA, and dementia; 1 leg pain due to radicular disease)</td>
<td>Not stated</td>
<td>Higher age at onset, longer duration of symptoms and “suspicion of neurological disorder” predicted misdiagnosis</td>
</tr>
<tr>
<td>2002</td>
<td>47</td>
<td>Prospective Neurological inpatients; 55% weakness, 45% sensory only; retrospective</td>
<td>12.5</td>
<td>1 case (intermittent paraparesis due to multiple sclerosis)</td>
<td>30% taken medical retirement; 38% limited in moderate activities; 43% with severe or very severe pain</td>
<td>Positive: sensory symptoms and signs alone rather than weakness and/or sensory symptoms</td>
</tr>
</tbody>
</table>

*Excluding studies with high proportions of other functional neurological symptoms, for example non-epileptic attacks, pain, non-organic visual symptoms.
**Length of time after assessment (mean 3.75 years after symptom onset).
†Two patients with visual symptoms and seven with pseudoseizure attacks also reported.
†Three studies report limited data on motor symptoms alone: Carter (1946): 22% unchanged or worse at five years; Ljungberg (1957): 32% unchanged or worse at five years; Maier and Trimm (1996): 34% not improved at 10 years.

with an average of nine current physical symptoms. Our data show that patients with functional weakness or sensory symptoms, who have been investigated as inpatients, have symptoms and disability that are often persistent in the long term. The comparison of the disability and distress data of our study population with locally acquired control groups indicates that they perform at a similar level to patients with multiple sclerosis (table 2) and considerably worse than those with “hysteria” (table 3). A study of patients referred to a specialist psychiatric service is a notable outlier with a rate of misdiagnosis of 13% (although there was a prior “suspicion of neurological disorder” in 80% of these “misdiagnosed” cases). Pooling the results of the four studies in table 3, in which the neurological misdiagnoses of patients with functional motor and sensory symptoms are described in detail, with the results from this study shows that there were 16 cases in 273 patients (6%). Other studies looking at the prognosis of conversion disorder have included significant numbers of patients with other functional neurological symptoms such as non-epileptic attacks and blindness. These are reviewed elsewhere and we do not elaborate on them here.

Misdagnosis is common in medicine. For example, reported rates of misdiagnosis in epilepsy vary from 26% to 42%. In a population based study of 387 subjects diagnosed with multiple sclerosis, 17% subsequently turned out to be wrongly diagnosed, half because they had another neurological disorder and half because the symptoms were “functional” or psychological in origin. Similar misdiagnosis rates have been reported in motor neurone disease (8%) and schizophrenia (6%). The process by which neurologists decide that weakness or sensory disturbance is functional or medically unexplained has come under remarkably little scrutiny. Despite this, our data suggest that this process is as least as accurate as the diagnosis of other neurological disorders.

Functional weakness and sensory symptoms only rarely develop into neurological disease

The prognosis of “hysteria” gained notoriety after an influential paper by Slater in 1965. Slater claimed that 61% of his cohort of patients with “hysteria” developed neurological disease. His analysis, however, is flawed and his conclusion that hysteria is a “delusion and a snare” is highly misleading. Although contemporaries, including Walshe, protested, the paper is often quoted in textbooks—perhaps because it is consistent with doctors’ fears about misdiagnosing symptoms as functional.

Slater’s views have been refuted by several recent studies reporting rates of misdiagnosis of between zero and 4% in regional and tertiary neurological centres (table 3). A study of patients referred to a specialist psychiatric service is a notable outlier with a rate of misdiagnosis of 13% (although there was a prior “suspicion of neurological disorder” in 80% of these “misdiagnosed” cases). Pooling the results of the four studies in table 3, in which the neurological misdiagnoses of patients with functional motor and sensory symptoms are described in detail, with the results from this study shows that there were 16 cases in 273 patients (6%). Other studies looking at the prognosis of conversion disorder have included significant numbers of patients with other functional neurological symptoms such as non-epileptic attacks and blindness. These are reviewed elsewhere and we do not elaborate on them here.
Unilateral functional weakness and sensory disturbance

Limitations
The original sample was of inpatients, potentially limiting the generalisability of the findings to outpatient practice (where the clinical presentation may be less severe or persistent). The excess of left sided symptoms (78%) in this cohort could, in the light of a recent systematic review in which only 58% were left sided, represent another source of bias, although there is insufficient published evidence to allow us to estimate its potential importance. The sample was also assembled retrospectively and so may not have been truly consecutive. The initial assessments were done as part of routine clinical practice, so they did not generate standardised data about the patients. In particular we did not have systematic information about the chronicity of symptoms, comorbidity of organic disease, and psychiatric disorders at the time of the initial investigation. Despite these limitations, we believe that the original sample was reasonably representative of general neurological practice in a teaching hospital at that time.

The sample followed up was incomplete. Incomplete follow up can be a further source of bias, particularly when an infrequent outcome such as a misdiagnosis is sought. The largest loss to follow up was the nine patients who had moved out of southeast Scotland and so could not be traced. Of the eight patients who were traceable but did not respond to the questionnaire, we know that six do not have a neurological disease (according to their family doctor), although it is unclear whether these patients are less or more disabled than the rest of the sample.

The follow up assessments were limited to self rated questionnaire responses by patients and three simple questions asked of their family doctors. The patients were not formally re-examined by a neurologist and we relied on the family doctor to detect new neurological disease. Although this means that mild cases of a disease such as multiple sclerosis may have been missed, it seems less likely that a family doctor would miss moderate or severe neurological disease.

Implications for clinical practice
The high frequency of long term symptom persistence, disability, and distress in this follow up of inpatients with functional weakness and sensory symptoms has important clinical implications. While it may be unhelpful to tell a patient with symptoms like this that they will not get better, it may be particularly true for those patients who, for whatever reason, come to be investigated as inpatients rather than as outpatients.

Doctors are sometimes reluctant to make a positive diagnosis of functional neurological symptoms. This may be because they fear it will delay a subsequent disease diagnosis, because they do not wish to offend the patient, or because they feel that there is no point in making this diagnosis because there is no treatment. There is only one published trial of treatment for functional weakness.25 This showed significant improvement in both arms of a multidisciplinary rehabilitation treatment (although no extra effect from hypnosis). Trials of cognitive behavioural therapy for other medically unexplained symptoms such as chronic fatigue have now shown that treatment can have a sustained and clinically significant effect.26

There is even some evidence that patients with chronic multiple symptoms can improve substantially with treatment.25 Furthermore, the recognition that a patient has long term vulnerability to developing functional somatic symptoms may, at the very least, be important in preventing future iatrogenic harm from unnecessary investigation and treatment.27

Conclusions
Patients admitted to a neurological ward with functional weakness or sensory disturbance are likely to continue to suffer symptoms, disability, and distress at long term follow up. They are, however, highly unlikely to develop a neurological disease that explains their presenting symptoms.

Prognostic studies of functional weakness and sensory symptoms have been scant, given the size of the clinical problem, and have suffered by focusing on the problem of misdiagnosis at the expense of symptom persistence and disability. Part of the problem is that investigators have defined cases using a psychiatric diagnosis of conversion disorder (and previously hysteria), rarely made by the neurologists who see most of the patients. Defining the clinical problem as a symptom rather than as a disorder allows greater generalisability of the findings to neurological practice. More prospective studies that examine the predictive power of aspects of the clinical assessment are needed to guide clinicians in deciding which symptoms are likely to persist and whether conservative or active management is most appropriate.

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