Brain (2001), **124,** 1077–1090

Functional neuroanatomical correlates of hysterical sensorimotor loss

P. Vuilleumier,[1,4] C. Chicherio,[2] F. Assal,[1] S. Schwartz,[3] D. Slosman[2] and T. Landis[1]

Departments of [1]Neurology and [2]Nuclear Medicine and Radiology, University Hospital of Geneva, [3]Institute of Psychology, University of Lausanne, Switzerland and [4]Institute of Cognitive Neuroscience, University College London, UK

Correspondence to: Dr P. Vuilleumier, MD, Institute of Cognitive Neuroscience, University College London, Alexandra House, 17 Queen Square, London WC1N 3AR, UK
E-mail: p.vuilleumier@ucl.ac.uk

Summary

Hysterical conversion disorders refer to functional neurological deficits such as paralysis, anaesthesia or blindness not caused by organic damage but associated with emotional 'psychogenic' disturbances. Symptoms are not intentionally feigned by the patients whose handicap often outweighs possible short-term gains. Neural concomitants of their altered experience of sensation and volition are still not known. We assessed brain functional activation in seven patients with unilateral hysterical sensorimotor loss during passive vibratory stimulation of both hands, when their deficit was present and 2–4 months later when they had recovered. Single photon emission computerized tomography using ^{99m}Tc-ECD revealed a consistent decrease of regional cerebral blood flow in the thalamus and basal ganglia contralateral to the deficit. Independent parametric mapping and principal component statistical analyses converged to show that such subcortical asymmetries were present in each subject. Importantly, contralateral basal ganglia and thalamic hypoactivation resolved after recovery. Furthermore, lower activation in contralateral caudate during hysterical conversion symptoms predicted poor recovery at follow-up. These results suggest that hysterical conversion deficits may entail a functional disorder in striatothalamocortical circuits controlling sensorimotor function and voluntary motor behaviour. Basal ganglia, especially the caudate nucleus, might be particularly well situated to modulate motor processes based on emotional and situational cues from the limbic system. Remarkably, the same subcortical premotor circuits are also involved in unilateral motor neglect after organic neurological damage, where voluntary limb use may fail despite a lack of true paralysis and intact primary sensorimotor pathways. These findings provide novel constraints for a modern psychobiological theory of hysteria.

Keywords: basal ganglia; conversion; hysteria; neuroimaging; thalamus

Abbreviations: AOI = area of interest; BA = Brodmann area; ECD = ethylenecysteinate dimer; rCBF = regional cerebral blood flow; ROI = region of interest; SPECT = single photon emission computerized tomography; SPM = statistical parametric mapping; SSM = Scaled Subprofile Model; T_1 = vibratory stimulation with symptoms present; T_2 = vibratory stimulation after recovery

Introduction

Patients with hysterical conversion disorders present with a loss or distortion of neurological function that cannot be fully explained by a known organic neurological disease (American Psychiatric Association, 1994). Yet, their symptoms are not intentionally feigned, not adequately explained by malingering, and may result in significant distress and handicap (Merskey, 1995). In clinical neurological practice, hysterical conversion symptoms represent a common disorder, accounting for 1–3% of diagnoses in general hospitals (Marsden, 1986), or even more in some neurological settings (Binzer and Kullgren, 1998; Ron, 1994). Such symptoms usually confront clinicians with several problems of management due to difficulties with definition, diagnosis, and therapeutic approaches (Ron, 1994), challenging a traditional division between neurology and psychiatry (Marsden, 1986; Trimble, 1996).

Hysterical symptoms long raised questions about mind–body relationships. Described in early medical writings as psychic disorders caused by bodily disturbances (e.g. displaced uterus in Antiquity), they were later regarded as the physical effect of violent impressions or passions (for review, see Merskey, 1995). One century ago, Charcot postulated a dysfunction of the nervous system produced by psychological factors and ideas through mechanisms similar

to hypnosis (Charcot, 1892). He classified hysteria as a neurosis, together with epilepsy, chorea and parkinsonism, in contrast to structural lesions. Janet further stated that 'fixed ideas' can arise outside consciousness and cause hysterical symptoms from a dissociation between cognitive and emotional processes that are normally integrated in the control of behaviour (Janet, 1894). The most influential contribution came from Freud, who emphasized the primary role of psychic motives, which he believed to be kept unconscious by repression, related to childhood trauma and sexuality, and transformed into symbolic physical complaints based on past experiences (Freud and Breuer, 1895). Current designation as 'conversion disorder' in modern psychiatric terminology still reflects these psychodynamic ideas (American Psychiatric Association, 1994). However, conversion and other hysterical conditions occur with a variety of psychosocial stressors not necessarily related to childhood or sexual difficulties, and their pathogenesis remains a matter of debate (Miller, 1987; Merskey, 1995; Halligan and David, 1999). A role of neurobiological factors is suggested by the fact that symptoms are more frequent on left-side limbs, pointing to possible right-hemisphere involvement (e.g. Stern, 1983), and seem occasionally facilitated by a real coexisting brain disease (e.g. Eames, 1992).

However, specific functional brain correlates of conversion symptoms have not been demonstrated, except for a few recent pioneering studies (Marshall *et al*., 1997; Spence *et al*., 2000). Over 100 years after Charcot and Freud, hysteria has generated many speculations but still few novel observations (for reviews, see Kihlstrom, 1994; Halligan and David, 1999). Purely psychodynamic accounts are now recognized as insufficient, but a modern theoretical framework is still lacking (Miller, 1987; Merskey, 1995; Halligan and David, 1999). Physicians, like philosophers, still often call upon a 'disease of the will' or 'of the imagination' (Merskey, 1995), yet little is known about the neural functioning of motor will or imagination, and how it may be affected in hysterical patients (Spence *et al*., 2000). Demonstrating objective brain correlates of hysterical symptoms may therefore help to understand the mechanisms that underlie a subjective experience of abnormal neurological function in these patients. Also, it may provide unique insights into mechanisms that subserve normal conscious experience of sensation and volition. A variety of neuropsychological findings (e.g. Flor-Henry *et al*., 1981) and neurophysiological abnormalities (e.g. Tiihonen *et al*., 1995; Marshall *et al*., 1997; Lorenz *et al*., 1998; Spence *et al*., 2000) have been reported in patients with hysterical conversion. However, many of these studies included only a few or single patients, and provided relatively conflicting or inconclusive results overall. Moreover, many other studies have emphasized normal findings using standard neurophysiological measures such as somatosensory or motor evoked potentials (e.g. Howard and Dorfman, 1986; Meyer *et al*., 1992).

The present study sought to determine whether there are specific neurophysiological markers associated with hysterical motor deficits in a group of seven patients who were prospectively selected from referrals to a general neurological clinic. We measured regional cerebral blood flow (rCBF) changes associated with the presence of strictly unilateral symptoms, using single photon emission computerized tomography (SPECT) during controlled sensorimotor conditions. We selected patients with acute conversion disorder without previous psychiatric diagnosis, who typically exhibit circumscribed deficits with good recovery and fewer comorbidities than patients with long-lasting deficits (Ron, 1994; Binzer and Kullgren, 1998).

Our study design introduced two important methodological features. First, cerebral activation was measured not only at rest, but also during a controlled stimulation involving bilateral vibration of both affected and unaffected limbs. Passive vibration provides selective inputs within proprioceptive pathways directly participating in motor control (e.g. Lackner and Di Zio, 1984), and it is known to elicit widespread activity in both sensory and motor areas through such afferents, including primary and secondary cortex, premotor areas and subcortical structures, even when subjects are not required to undertake an active motor task (Seitz and Roland, 1992; Coghill *et al*., 1994; Yousry *et al*., 1997). Abnormal neural response to vibration can be observed in a variety of neurological diseases that affect either sensory or motor function, including extrapyramidal movement disorders that are characterized by difficulties in voluntary motor function without true paralysis (e.g. Tempel and Perlmutter, 1990). We expected that passive vibration might thus enable us to probe the functional state of activity and responsiveness of distributed motor and sensory circuits in a symmetric and controlled manner, while avoiding some confounds due to the possible variability or unreliability in performing an active task. In contrast, previous studies required patients to execute voluntary movements with their affected (paralysed or weak) limbs (e.g. Marshall *et al*., 1997; Spence *et al*., 2000). Although requiring active movements might be expected to recruit more specifically volitional motor processes that are presumably affected in hysterical paralysis (e.g. Halligan and David, 1999), there are potential problems related to the ambiguity of such instructions in patients who actually complain of an inability to move, as well as to the many possible differences in strategy, effort and conflict reaction that may be brought into play by different individual subjects in such conditions.

A second novel feature was that we compared brain activation when the patients' conversion deficit was present, and then a few weeks later when it was resolved, so that the patients could serve as their own controls and rCBF changes could be directly correlated with the presence of hysterical symptoms. Such a repeated test/retest design within the same individuals has proved to be crucial in complex psychiatric conditions in order to distinguish between state (symptom) or trait (comorbidity) abnormalities (Ebert and Ebmeier, 1996; Frith and Dolan, 1998). In summary, our main goal was to determine regions in motor and sensory systems that

would show asymmetric activation in response to vibratory stimulation, specifically associated with the presence of subjective sensorimotor symptoms during hysterical conversion.

Methods

Patients

Seven patients admitted in our hospital were prospectively selected during a 2-year period (1996–1997), including six females and one male (age 16–54, mean 35.1 years, all right-handed except one). Criteria for inclusion were a strictly unilateral loss of motor function of recent onset (<2 months), with or without concomitant sensory disturbances in the same limb, clearly due to psychogenic factors, and in the absence of any present or past neurological disease (American Psychiatric Association, 1994). Patients with additional complaints (e.g. bilateral deficits, vision disturbances, vertigo), long-lasting deficits (>2 months), past medical problems or other major psychiatric illness were excluded. No patient was under psychotropic medication at the time of presentation. Subjective paralysis and weakness were predominant symptoms in all cases, but often accompanied by superficial sensory disturbances such as numbness or dysaesthesia (six out of seven patients, see Appendix I). The upper limb (one case), lower limb (one case) or both limbs (five cases) were involved on one side of the body (four left and three right).

Neurological and psychiatric diagnoses were made by physicians independent to the study. Organic pathology of the central or peripheral nervous system was excluded in all cases by negative neurological examination, as well as detailed radiological imaging and electrodiagnostic investigations, including normal brain MRI (seven cases) or spine MRI (three cases), normal neurophysiological tests (somatosensory, motor and visual evoked potentials in seven, five and five cases, respectively; EMG in three; carotido-vertebral Doppler in three), normal laboratory and immunological tests (including CSF in five cases), and positive psychiatric assessment suggesting a conversion disorder according to DSM-IV criteria (American Psychiatric Association, 1994). All patients faced stressful life events (see brief case histories in Appendix I). Psychiatric assessment noted acute or chronic stress factors (DSM-IV axis 4) in all cases, depressed mood in five, and unspecified personality disorder (DSM-IV axis 2) in one.

All patients were followed-up for 6–12 months after initial admission. All of them improved with supportive physiotherapy and psychotherapy. Four patients had no symptom on follow-up 3–6 months after admission (V.U., T.A., V.A., B.R.), while three others had milder but persisting or new complaints after 12 months (L.M., R.O., L.A.). Informed consent was obtained from all subjects and the study was approved by the University Hospital of Geneva.

Imaging procedure

SPECT scans were obtained in three different conditions on separate sessions: during baseline resting state with subjective deficit present (B scan, seven cases); during bilateral vibratory stimulation with subjective deficit present (T_1 scan, seven cases) a few days later (2–4 days, mean 2.8); and during the same stimulation after recovery from deficit (T_2 scan, four cases) 2–4 months later (8–18 weeks, mean 14.3). Three patients who had persisting or new complaints at follow-up after 6 months had no T_2 scan. In T_1 and T_2 scans, vibratory stimulation (50 Hz) was symmetrically applied to both affected and unaffected limbs (hands in six cases; feet in one case, Patient B.R.) using the same vibratory devices, passively attached to the hands or feet. Patients lay down in the supine position in a darkened and silent room, with eyes closed and ears plugged. A single bolus of 740 MBq of ethylenecysteinate dimer (ECD) labelled with Technetium-99m (^{99m}Tc-ECD) was injected for each of the three scan session; note that ECD tracer is more reliable than others [e.g. HMPAO (hexa-methyl-propylene-amino-oxime)] for discrete regional changes and depends not only on CBF but also on cerebral metabolism (Shishido *et al*., 1995). At T_1 and T_2, vibration was administered for 3 min before injection and lasted 3 min more afterward. SPECT scans were obtained 20 min after injection on a 3-heads Toshiba CGA-9300 camera with fan beam collimators and simultaneous acquisition of the ^{153}Gd-rod source for transmission and scatter correction (Billet and Slosman, 1998). Data were acquired and reconstructed in a 128×128 matrix. The whole brain volume was covered. Scatter correction used a Shepp and Logan filter and transmission correction was applied using the ^{153}Gd transmission scan. Images were reconstructed in sagittal, coronal and transaxial planes from the orbitomeatal line with a slice thickness of 2 pixels (32 slices).

SPECT data were analysed using two different statistical methods, allowing to combine inferential and descriptive approaches suitable to a small sample size, and independent cross-checking of the results without relying on an *a priori* hypothesis (see Pawlik, 1991). Regional changes in perfusion between conditions were first assessed by parametric analyses on a voxel-by-voxel basis across the whole group of patients, following standard statistical parametric mapping methodology (SPM; Friston *et al*., 1995), as described below. This was supplemented by independent non-parametric analyses applied to regions of interest on a multiple single case basis, using Scaled Subprofile Model (SSM) (Alexander and Moeller, 1994), also as described below. Since the side of deficit differed across patients (left versus right limb deficits), all analyses were done after realigning scans onto the side of symptoms (contralateral versus ipsilateral hemisphere) unless stated otherwise.

Statistical parametric mapping

Statistical parametric mapping was performed using SPM96 (Wellcome Dept of Cognitive Neurology, London, UK)

(Friston *et al*., 1995) implemented in MATLAB (Mathworks Inc., Sherborn, Mass., USA), after data from reconstructed scans were spatially transformed and flipped according to the side of deficit. The different images from each patient were realigned to the first, creating a mean volume of resliced scans, and applying a linear 9 parameters affine transformation. Images were normalized into a standard space (Talairach and Tournoux, 1988) and smoothed with an isotropic Gaussian kernel (full-width half-maximum of 16 mm) to accommodate intersubject differences in gyral anatomy and suppress high frequency noise. Analysis of covariance was applied to count densities on a voxel by voxel basis, with proportional scaling to remove differences in global activity within and between patients. Changes in rCBF were represented by a linear contrast of the means across conditions on a voxel by voxel basis using the *t*-statistic. The resulting sets of *t*-values constituted the statistical parametric map SPM *t*. SPM *t*-values were transformed to the unit normal distribution SPM(*Z*) with *Z* scores $\geqslant 3.09$ ($P < 0.005$ uncorrected for multiple comparisons) to identify significant changes between conditions, and only activation foci with corrected significance of $P \leqslant 0.01$ at the cluster level were reported. There were two planned comparisons of interest: (i) activation during T_1 scan (with vibratory stimulation) versus baseline (resting state), assessing the effect of bilateral vibratory inputs in the presence of unilateral deficits in sensorimotor function; and (ii) activation during T_2 scan (symptoms recovered) versus activation during T_1 scan (symptoms present), assessing the changes in cerebral activity associated with changes in sensorimotor function.

Region of interest segmentation

Cerebral cortex and subcortical nuclei were segmented into several small, symmetrical regions of interest (ROIs) by a semi-automated procedure (see Hellman *et al*., 1989), and mean count density, standard deviation and pixel size were then measured in these ROIs. On each axial slice, a cortical rim was first determined using a standardized threshold based on whole brain median count value to define the outer edge and a fixed width from the latter to define the inner edge, and then divided into equal ROI segments (6–8 per hemisphere) on 18 consecutive slices. Symmetrical elliptical ROIs were also placed on other regions not captured by this procedure (temporal poles, medial and orbital frontal lobes, thalamus, caudate and lenticular nuclei; 3–6 ROIs per hemisphere each). The resulting ROIs segments were subsequently grouped into 20 anatomically defined areas of interest (AOIs) and their mean count densities were averaged, correcting for segment size. The same ROIs matched across hemispheres and scans in a given subject were selected for AOI analysis (about equal number across subjects). In total, 180–186 segments in each hemisphere were grouped in 20 cortical and subcortical AOIs, including motor [Brodmann area (BA) 4, 10–13 ROIs], premotor (BA 6, 9–11; BA 8, 8–10), prefrontal (BA 9–44, 8; BA 45, 8; BA 46, 8–10; BA 10, 6–9; BA 11, 4–8), medial frontal (BA 6–24–32, 5), sensory (BA 1–2–3, 18–20), posterior parietal (BA 7, 14–16; BA 39–40, 18–19), temporal (BA 37, 14–16; BA 22, 9–12; BA 20–21, 6–12; BA 38, 8–10), occipital (BA 17–18–19, 8–10) and subcortical regions (caudate, 5–6; lenticular nuclei, 3–4; thalamus, 5–6).

Hemispheric asymmetries (contralateral versus ipsilateral) and recovery changes (T_2 versus T_1) were assessed by pairwise non-parametric comparisons between homologous AOIs, using regional count densities extracted from ROIs, normalized to whole brain mean (Wilcoxon test with $P \leqslant 0.01$; all reported comparisons correspond to $P \leqslant 0.002$ uncorrected using *t*-tests, $P < 0.05$ corrected for multiple comparisons; for advantages of non-parametric tests with small sample size, see Pawlik, 1991). Asymmetry percentages were computed using mean count differences between homologous ROIs in the two hemispheres for each scan [% = (contralateral – ipsilateral)/(contralateral + ipsilateral) × 200], and change percentages were computed using count differences between T_1 and T_2 scans in homologous ROIs for each hemisphere [$\% = (T_2 - T_1)/(T_2 + T_1) \times 200$].

Scaled Subprofile Model

Raw data from all AOIs were entered into SSM analysis to determine patterns of activation across scans and patients (Alexander and Moeller, 1994). SSM is a statistically robust method that applies a modified principal component analysis, allowing detection of simultaneous networks of regions that form significant covarying patterns (topographic profiles) associated with a specific state, and to measure how the expression of such regional patterns may differ not only between different scans but also between hemispheres or subjects (see Alexander and Moeller, 1994). Thus, when different subjects (or hemispheres) manifest particular covariance patterns to a greater or lesser degree, SSM can compute loading scores that quantify the representation of this pattern in each subject (or hemisphere). Such a method is particularly suitable to assess patterns of activity and temporal changes using repeated measures in a small sample of subjects (see Eidelberg *et al*., 1996).

SSM was performed using data from our 20 AOIs to create a 20 region × 16 hemisphere matrix (each scan/subject), as described in detail elsewhere (Alexander and Moeller, 1994). Briefly, the SSM analysis comprises a series of 16 observations, including T_1 and T_2 data from all AOIs of the two hemispheres, in the four subjects who recovered, entered into the analysis without any *a priori* specification about the possible relevant conditions (i.e. before or after recovery, contralateral or ipsilateral side). After all region × hemisphere data in the matrix are log transformed, the mean values across regions are first subtracted from each hemisphere value, and the mean values across hemisphere are then subtracted from each regional value, thus resulting in a twice normalized matrix of residual profiles. The latter is subsequently used to compute two separate region × region

Table 1 *Coordinates and magnitude of maximal rCBF changes in SPM analysis*

Brain side	Brodmann area	*x*	*y*	*z*	*Z*-score
rCBF changes associated with bilateral vibrotactile stimulation					
$T_1 > B$					
Contra	Middle prefrontal gyrus (BA 6)	–34	14	52	4.27
Contra	Middle prefrontal gyrus (BA 8)	–32	50	0	3.28
Contra	Middle prefrontal gyrus (BA 8)	–32	34	38	3.15
Contra	Superior prefrontal gyrus (BA 9/46)	–26	46	28	2.99
Contra	Post-central gyrus (BA 1/2)	–34	–26	46	4.19
Contra	Post-central gyrus (BA 5)	–8	–40	60	3.50
Contra	Superior parietal lobule (BA 7)	–22	–42	58	3.14
Ipsi	Superior prefrontal gyrus (BA 9/46)	40	28	36	3.85
Ipsi	Middle prefrontal gyrus (BA 46)	36	44	16	3.85
Ipsi	Superior prefrontal gyrus (BA 9)	22	50	52	3.36
Ipsi	Superior prefrontal gyrus (BA 8)	0	30	58	3.34
Ipsi	Paracentral lobule (BA 5)	16	–32	56	3.13
Ipsi	Post-central gyrus (BA 1/2)	28	–32	48	3.03
$B > T_1$					
Contra	Cuneus/medial occipital gyrus (BA 19/18)	–18	–98	14	4.27
Ipsi	Inferior occipital gyrus (BA 18)	26	–86	–2	4.17
Ipsi	Lingual gyrus (BA 18)	22	–74	4	4.10
Contra	Inferior occipital gyrus (BA 18/19)	–38	–80	–8	3.25
Ipsi	Lingual gyrus (BA 18)	4	–76	–6	3.24
rCBF changes associated with unilateral sensorimotor symptoms					
$T_2 > T_1$					
Contra	Putamen	–20	12	–4	5.14*
Contra	Thalamus	–10	–2	4	4.09*
Contra	Caudate nucleus	–14	–6	20	3.81*
$T_1 > T_2$					
Ipsi	Post-central gyrus (BA 1/3)	30	–32	80	3.87
Ipsi	Precentral gyrus (BA 6/4)	36	–12	72	2.87

B = baseline resting state with symptoms present; T_1 = vibratory stimulation with symptoms present; T_2 = vibratory stimulation after recovery; contra/ipsi = hemisphere contralateral/ipsilateral to symptoms; BA = Brodmann area; *x*, *y* and *z* (in millimetres) are coordinates in the stereotactic space of Talairach and Tournoux (1988). *$P < 0.005$ corrected for the cluster.

and hemisphere × hemisphere covariance matrices. These are then entered in a principal components analysis performed without rotation to obtain a set of regional patterns and the corresponding loading of each hemisphere/subject, respectively. Here again, our goal was to identify whether any patterns of regional activity changed with the presence or absence of deficit.

Results

SPM analysis

We first assessed the effects of symmetric sensorimotor stimulation at the time of unilateral conversion symptoms using SPM across the whole group of patients (Table 1). Compared with resting state (B), bilateral vibratory stimulation in the presence of subjective paralysis (T_1) produced significant rCBF increases in both hemispheres in the parietal somatosensory cortex (bilateral BA 1/2/3 and 5, contralateral BA 7), frontal premotor cortex (bilateral BA 8, contralateral BA 6) and anterior prefrontal areas (bilateral BA 9/46, contralateral BA 10; Fig. 1A). These activations correspond to the locations found in PET studies using hand vibration in normal subjects (Seitz and Roland, 1992; Coghill *et al*., 1994; Yousry *et al*., 1997), and confirm that our vibratory stimulation induced reliable activity in both sensory and motor systems (Tempel and Perlmutter, 1990; Yousry *et al*., 1997). There were no reliable asymmetries in cortical activity elicited by vibration between hemispheres contralateral and ipsilateral to the symptoms, except for slightly greater responses in contralateral superior parietal cortex. Visual areas showed bilateral rCBF decreases during stimulation (Table 1).

We then examined the changes associated with recovery. Significant differences were observed between presence and absence of conversion deficit in those four patients who had no symptoms at follow-up (Fig. 1B–D). When patients experienced their subjective motor deficits (T_1), rCBF during vibration was decreased in the contralateral thalamus and basal ganglia (caudate and putamen) compared with when the deficit was resolved (T_2), while it was increased in the ipsilateral somatosensory (BA 1/3) and premotor (BA 6)

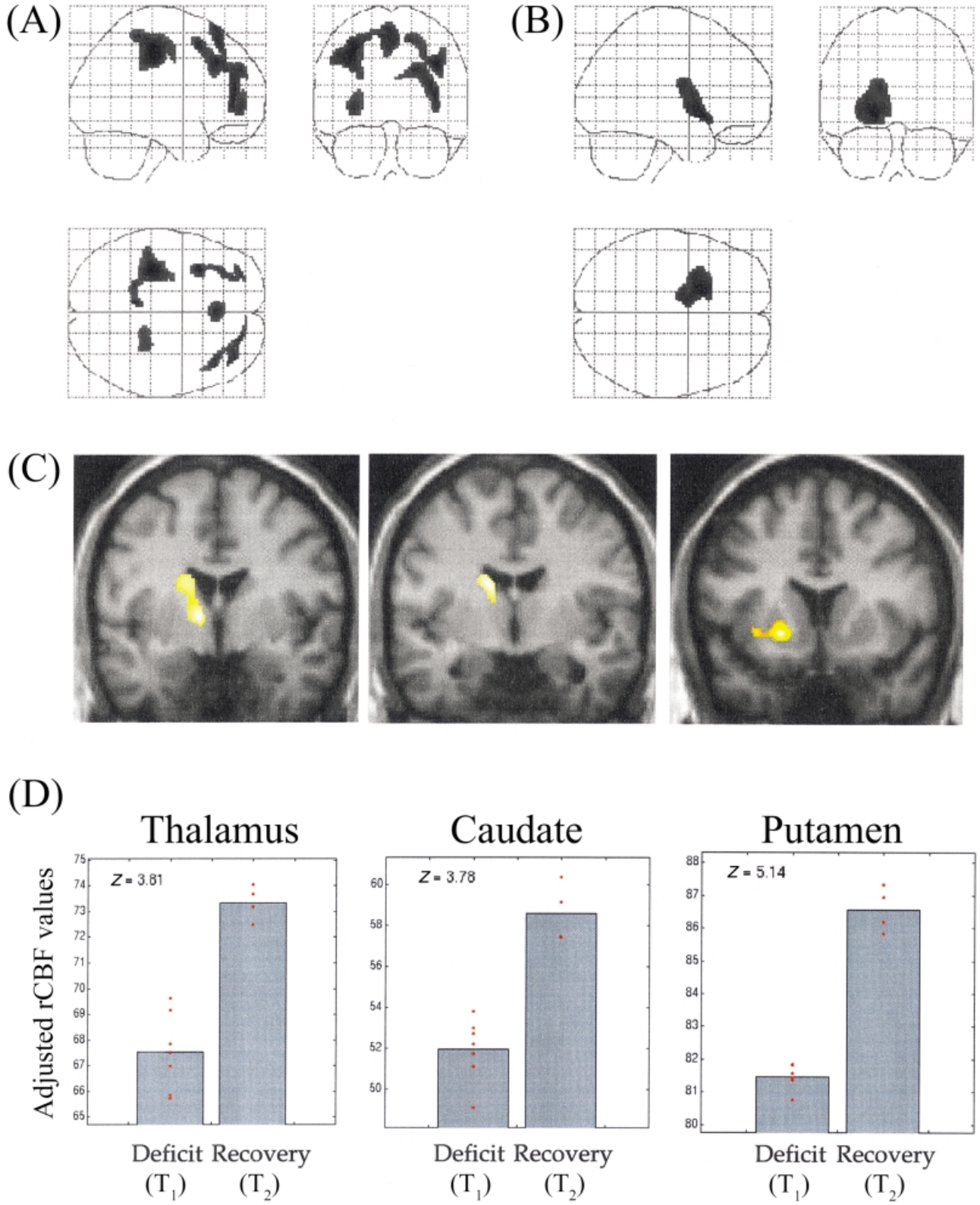

Fig. 1 Statistical parametric maps of significant rCBF changes. (**A**) Increased activity in bilateral frontal and parietal cortical regions when bilateral vibration stimulation was compared with resting state during unilateral hysterical symptoms ($T_1 > B$). (**B**) Increased activity in basal ganglia and thalamus contralateral to the deficit when bilateral vibration after recovery was compared with the same stimulation during symptoms ($T_2 > T_1$). (**C**) rCBF changes in the thalamus ($y = -2$ mm) and basal ganglia (–6 mm, caudate; –12 mm, putamen) superimposed on a coronal MRI template in normalized stereotactic coordinates (Talairach and Tournoux, 1988). (**D**) Adjusted mean rCBF equivalents (grey bars) and individual data points (red dots) at the maxima of changes in the basal ganglia and thalamus in the presence and after recovery of symptoms. Exact coordinates are given in Table 1.

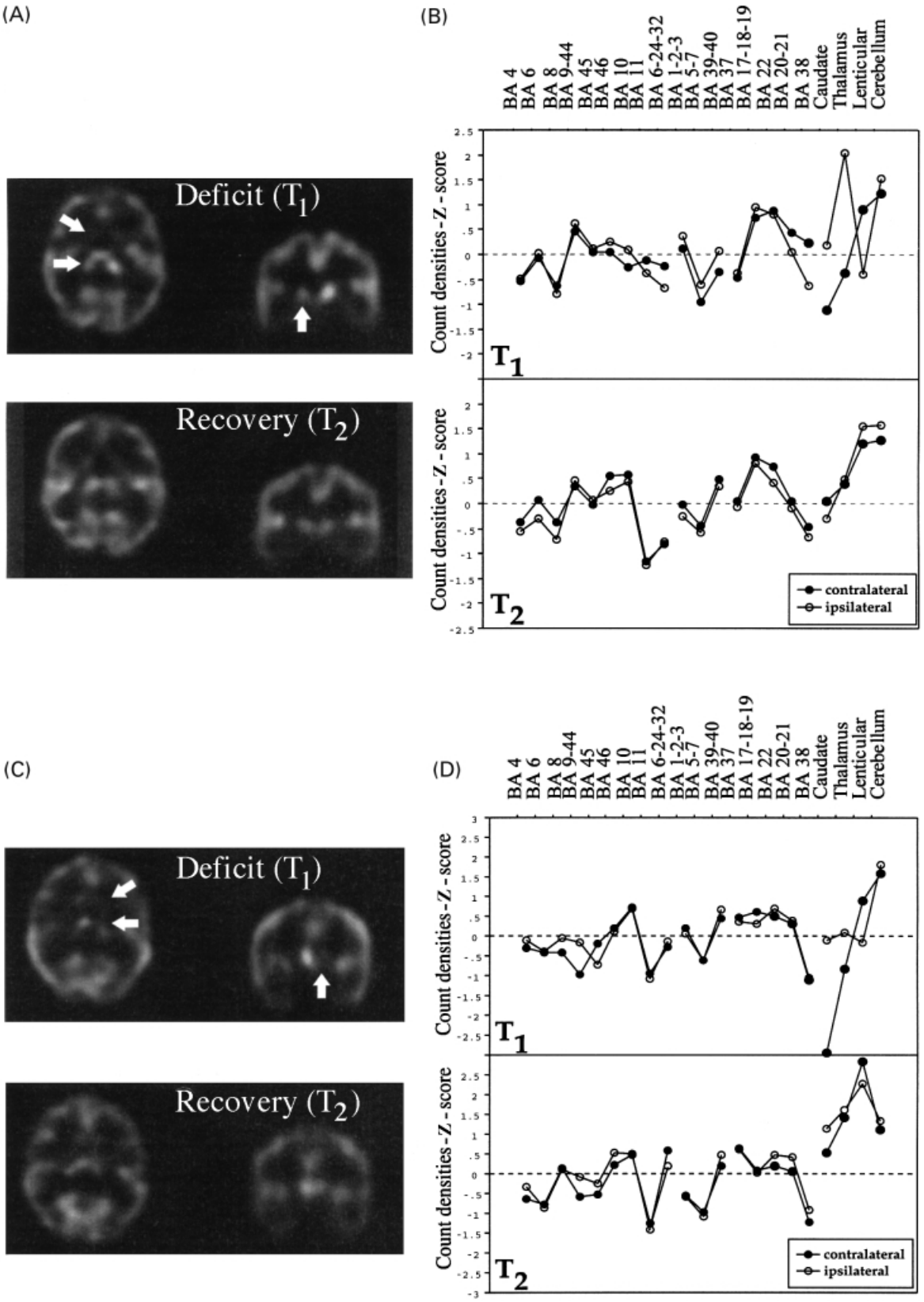

Fig. 2 Illustration of SPECT data in two patients with hysterical sensorimotor loss in the left arm (**A** and **B**) and right arm and leg (**C** and **D**), respectively. (**A** and **C**) Raw images (axial and coronal slices) obtained during bilateral vibratory stimulation of the hands show lower activity in the thalamus and caudate contralateral to the symptoms (T_1), resolving after recovery (T_2). (**B** and **D**) Average regional perfusion values measured from regions of interest (converted in *Z*-scores, normalized for each scan separately). Contra/ipsi = hemisphere contralateral/ipsilateral to subjective deficit. Similar results were obtained in other patients.

Table 2 *Topographical profiles in SSM analysis*

	Factor 1	Factor 2	Factor 3
Eigenvalue	5.46	2.24	2.14
% variance explained	45.5	18.6	17.9
(A) Brain areas			
BA 4	0.84		
BA 6	0.90		
BA 8	0.88		
BA 9–44	–0.65		
BA 44–45	–0.58	0.66	
BA 46			
BA 10	–0.75		
BA 11	0.66		
BA 6–24–32	0.7		
BA 1–2–3	0.87		
BA 5–7	0.97		
BA 39–40	0.57	0.68	
BA 37	–0.53	0.76	
BA 17–18–19			
BA 22	–0.72		
BA 20–21	–0.75		
BA 38	–0.55	–0.82	
Caudate	0.68		
Lenticular	–0.92		
Thalamus	0.72		
(B) Hemisphere (mean across subjects)			
T_1-contralateral	0.43	–0.06	0.58
T_1-ipsilateral	0.59	0.37	0.21
T_2-contralateral	0.77	–0.07	–0.24
T_2-ipsilateral	0.80	–0.11	–0.26

Factors indicate overlapping functional networks of brain areas whose activity is covarying across subjects and scan sessions (T_1 and T_2 = bilateral hand vibratory stimulation during subjective deficit and after recovery, respectively). Coefficients indicate the degree to which brain regions (A) and individual hemispheres (B) contribute to (or 'weigh' in) each topographical profile. For clarity, factor loadings <0.5 in topographical profiles are not shown.

cortex (Table 1). Such changes in contralateral thalamic and caudate activity associated with recovery from conversion symptoms were found in each individual patient (Figs 1C and 2; and see ROI analysis below).

For completeness, statistical parametric comparisons were also performed on scans not realigned onto the side of symptoms. This revealed no additional changes associated with vibratory stimulation or presence of symptoms, which might have been related to some general right versus left hemispheric factors independent of the side of deficit.

ROI and SSM analysis

Consistent changes in thalamic and caudate activity, contralateral to conversion symptoms were confirmed by independent multiple single-case analyses in which we compared T_1 and T_2 scans in individual subjects who underwent both scanning sessions. SSM factorial analysis was performed on 20 anatomically defined AOIs to determine covarying topographic patterns of activity in the contralateral and ipsilateral hemispheres across scans and across subjects (see Methods). SSM extracted three main topographical profiles accounting for 82% of the data variance (Table 2A). The first factor reflects a predominant activation of primary and secondary sensorimotor areas in frontal and parietal lobes (BA 4, 6, 1–2–3, 5–7 and 39–40), with relative deactivation of lenticular nuclei and temporal lobe (BA 37–38). Loading coefficients (Table 2B) indicate that this pattern was expressed on both sides except for the hemisphere contralateral to the deficit in scan T_1. The second factor also reflects a network of prefrontal and parietal areas, loading more on the ipsilateral hemisphere during scan T_1. The third factor indicates a regional pattern that includes the thalamus, caudate and ventral frontal areas (BA 11, 44–45), which characterizes the hemisphere contralateral to the deficit in scan T_1.

To examine further the changes in activity and hemispheric asymmetry across the different scan conditions, paired comparisons between homologous brain areas were performed within individual subjects using average count densities in AOIs, normalized to whole brain mean. When sensorimotor symptoms were present (T_1), asymmetries in subcortical regions during vibratory activation were significant in each subject, with a relative hypoactivation of the contralateral thalamus (–9 to –19%, mean 12.6; $Z \geqslant 3.06$, $P < 0.005$ in each case, Wilcoxon paired rank test) and contralateral caudate (–6 to –30%, mean 15.9; $Z \geqslant 2.81$, $P < 0.005$), together with a relative hyperactivation of the contralateral lenticular nucleus (+9 to +11%, mean 9.9; $Z \geqslant 2.58$, $P < 0.01$). Only one patient (T.A.) showed a significant asymmetry in the post-central somatosensory cortex (BA 1/2/3, $Z = 4.01$, $P < 0.005$) and precentral motor cortex (BA 4, $Z = 3.06$, $P < 0.005$). In addition, a relative hyperactivation of the contralateral anterior temporal pole (BA 38, right hemisphere, Fig. 2B) was found in two cases ($Z \geqslant 2.52$, $P < 0.01$).

None of these asymmetries were seen after recovery (T_2). Compared with T_1, average normalized perfusion on T_2 scans significantly increased for each patient in contralateral thalamus (+7 to +23%, mean 18%; $Z \geqslant 3.07$, $P < 0.005$ in each case) and contralateral caudate (+12 to +36%, mean 22%; $Z \geqslant 2.81$, $P < 0.005$), much more than ipsilaterally (thalamus –12 to +14%, mean +4.6%, and caudate –5 to 14%, mean +7%, respectively). Two patients (T.A. and V.A.) also showed slight but significant decreases in somatosensory cortex (BA 1/2/3), both contralaterally ($Z \geqslant 2.58$, $P < 0.01$) and ipsilaterally ($Z \geqslant 3.35$, $P < 0.005$). In addition, significant changes associated with recovery were observed in prefrontal areas (BA 46 and/or 6), with moderate but systematic increases ($Z \geqslant 2.66$, $P < 0.01$) contralateral to the deficit in two patients (V.U. and T.A.) and ipsilateral in one (V.A.), i.e. in the right hemisphere in all three cases. In fact, this resulted in a significant prefrontal asymmetry with relative left hypoactivation in all of these three patients after recovery ($Z \geqslant 2.66$, $P < 0.01$), whereas no such asymmetry was noted during symptoms. No other asymmetries or changes were remarkable.

Prediction of recovery

Since a few patients showed a lack of significant improvement in their symptoms at follow-up, we examined whether the degree of functional abnormalities in brain activation during initial symptoms was correlated with differential recovery. The three patients who had persisting deficits or new symptoms at follow-up had significantly lower activity in the contralateral caudate nucleus AOI during T_1 scan (mean normalized count densities ± SD were 67.97 ± 2.17) as compared with the other four patients who had complete recovery (mean 84.59 ± 8.09; Mann–Whitney $U = 12$, $P = 0.034$), while activity in the contralateral thalamus AOI was also marginally lower (mean 89.67 ± 1.75 versus 95.84 ± 2.39; Mann–Whitney $U = 11$, $P = 0.078$). By contrast, there was no significant difference in ipsilateral caudate activation (mean 97.97 ± 6.39 versus 96.91 ± 4.64) and ipsilateral thalamic activation (mean 96.53 ± 5.38 versus 106.08 ± 7.09) between the two groups of patients (Mann–Whitney $U = 8$, $P = 0.48$ for both comparisons). These data suggest that patients with a greater asymmetry in subcortical grey nuclei during symptoms might be less likely to show rapid recovery, although interpretation of this finding is clearly limited by the small number of cases.

Discussion

These results demonstrate a systematic neural correlate of focal hysterical conversion disorder, involving the basal ganglia and thalamus. This provides the first direct evidence of functional abnormalities in sensorimotor pathways specifically related to the presence of subjective neurological symptoms. Both SPM and SSM findings converged to show that transient unilateral sensorimotor loss of hysterical origin was associated with a relative hypoactivation of contralateral thalamus and basal ganglia circuits during bilateral hand vibration (T_1), regressing with recovery (T_2). Complementary evidence from independent statistical methods, involving voxel-based group analysis and ROI-based multiple single-case analysis, respectively, lends strong support to these results, with both types of methods similarly indicating that such significant subcortical changes were found in all of our patients. Changes in contralateral basal ganglia activity between T_1 and T_2 cannot be explained by sessional effects due to repeated scans, since repetition effects would not explain such asymmetrical changes. Also, lower activation in contralateral caudate during hysterical conversion symptoms predicted poor recovery at follow-up. In contrast, somatosensory and premotor cortical areas were still activated by vibration relatively symmetrically on both sides despite the presence of symptoms, consistent with objectively intact neurological function and normal cortical responses in motor or sensory evoked potentials, as typically observed in hysterical patients (Howard and Dorfman, 1986; Meyer *et al*., 1992). Only a mild asymmetry in the covariance patterns of frontoparietal networks was indicated by SSM and SPM analyses in the hemisphere contralateral to the deficit. Thus, activations induced by vibration were slightly greater contralaterally than ipsilaterally during symptoms (T_1–B), but decreased ipsilaterally more than contralaterally with recovery (T_1–T_2), suggesting a lower baseline activity, but preserved response to vibration in frontal and parietal cortex during symptoms. This would be consistent with an abnormal modulation from subcortical circuits in the thalamus and basal ganglia (Steriade and Llinás, 1988; Tempel and Perlmutter, 1990; Rossini *et al*., 1998), and possibly some secondary interhemispheric imbalance (Ferbert *et al*., 1992; Seyal *et al*., 1995).

Basal ganglia and thalamus are intimately connected within neural circuits or 'loops' that subserve both motor and cognitive functions (Alexander *et al*., 1986; Graybiel *et al*., 1994). In particular, striatothalamocortical premotor loops are critically involved in generating intentional movements and learning adaptive motor programmes (Graybiel *et al*., 1994), and their activity may contribute to the subjective sense of motor volition and effort (Gandevia, 1987). Neurological dysfunction in these circuits can cause a variety of motor and neuropsychiatric illnesses, such as parkinsonism, chorea, tics or obsessive–compulsive disorders, all implicating abnormal control of cortical function by basal ganglia–thalamic systems (Alexander *et al*., 1986; Bhatia and Marsden, 1994; Rauch and Savage, 1997). The thalamus is also strategically placed to modulate sensory and motor signals as it is the main relay of afferents to the cortex, and it may control the selective engagement of cortical areas involved in motor and cognitive functions via the intralaminar and reticular nuclei systems (Steriade and Llinás, 1988; Strafella *et al*., 1997).

Spatial resolution of SPECT does not permit definite demonstration of which part of the thalamus was more specifically affected in our patients. Notably, however, stimulation of central thalamic nuclei can trigger movements experienced as volitional by the subject (Hécaen *et al*., 1949), or inhibit voluntary action (Strafella *et al*., 1997), whereas their lesion (e.g. strokes) often cause 'intentional' motor neglect (Watson *et al*., 1978; Laplane *et al*., 1986; von Giesen *et al*., 1994) in which patients fail to use their affected limbs or behave like hemiplegics despite normal strength and sensation. Motor neglect is thought to reflect a dysfunction in striatothalamic circuits mediating motor preparation and intention (Watson *et al*., 1978; Laplane *et al*., 1986; von Giesen *et al*., 1994), and if associated with real paralysis, such a loss of intention may impede awareness of motor function and contribute to anosognosia for hemiplegia (Gold *et al*., 1994; Vuilleumier, 2000). In this respect, our findings in patients with hysteria (who experience a deficit in the absence of physical damage) offer an intriguing counterpart to the findings in neurological patients with anosognosia (who lack awareness of deficit following brain damage): in both instances, there is a discrepancy between awareness in the patient and objective neurological function, and striatothalamic disturbances are implicated in the abnormal

conscious behaviour, independent of an integrity of primary sensorimotor pathways. Taken together, these findings support previous theoretical proposals suggesting that attentional or motivational mechanisms might operate at the level of thalamus or basal ganglia to influence sensorimotor processes in hysterical conversion (Ludwig, 1972; Trimble, 1996), as well as in other disorders of intentional motor behaviour (Mogenson *et al*., 1980; Schultz, 1999; Brown and Pluck, 2000).

Remarkably, the basal ganglia have a unique position within premotor pathways in that their activity is especially dependent on environmental context cues and reinforcing motivational values (Graybiel *et al*., 1994; Kawagoe *et al*., 1998). The caudate nucleus receives prominent limbic inputs from the amygdala and orbitofrontal cortex, encoding emotional significance of events in relation to past experience, and thus contributes to elicit or suppress specific patterns of motor behaviour in response to emotional states (Rolls, 1995). Direct limbic inputs from amygdala and orbitofrontal cortex are also provided at the thalamic level, allowing the modulation of striatocortical loops based on affective cues (Mogenson *et al*., 1980). An influence of limbic signals on striatothalamocortical circuits has been implicated in motor or cognitive inhibition associated with several neurological or psychiatric disorders, such as apathy and depression (Bhatia and Marsden, 1994; Rauch and Savage, 1997; Brown and Pluck, 2000). In animals, alert states with inhibition of volitional behaviour (Rougeul-Buser *et al*., 1983; Rolls, 1995) and protective limb immobility after an injury (De Ceballos *et al*., 1986) are also known to implicate inhibitory processes in striatal and thalamic control of motor function. A role of these subcortical circuits in hysterical conversion therefore lends strong support to the view that they may derive from primitive psychobiological adaptive mechanisms or stereotyped illness behaviour with self-preservation value (Miller, 1987; Merskey, 1995), somehow similar to instinctive freezing or immobilization reaction in response to perceived threats (Kretschmer, 1948; Ludwig, 1972). We would suggest that hysterical paralysis might build upon such neural mechanisms to establish a selective inhibition of action through the modulation of specific basal ganglia and thalamocortical systems, with such inhibition being possibly triggered outside conscious will by various emotional stressors, through limbic inputs from amygdala and orbitofrontal cortex (Graybiel *et al*., 1994; Marshall *et al*., 1997). Decreased activity in basal ganglia–thalamic circuits might set the motor system in a functional state characterized by impaired motor readiness and initiation, resulting in abnormal voluntary behaviour.

Our patients were all selected on the basis of limited unilateral motor deficit, but most of them also had concomitant sensory disturbances in the same limb, mostly dysaesthesia or hypoaesthesia. Such sensory symptoms are commonly associated with conversion paralysis (Marsden, 1986; Merskey, 1995; Trimble, 1996). Therefore, our findings might reflect not only motor but also sensory hysterical deficits in these patients. Further research is needed to determine whether sensory and motor symptoms may relate to distinct thalamic or basal ganglia abnormalities. Recent studies have shown that both the thalamus (e.g. Iadarola *et al*., 1995; Tracey *et al*., 2000) and basal ganglia (e.g. Tempel and Perlmutter, 1990; Chudler and Dong, 1995; Rossini *et al*., 1998; Tracey *et al*., 2000) are implicated in normal or abnormal sensory integration and pain processing. Notably, combined changes in thalamic and basal ganglia activity are associated with an alteration of subjective sensation in patients with fibromyalgia (Mountz *et al*., 1995) and during acupuncture treatment (Hui *et al*., 2000), two conditions where both physiological and motivational factors are presumably involved.

One limitation of recovery findings in our study is that they applied to only four subjects who eventually recovered from their symptoms during a 2-year follow-up. However, our study includes the largest series of patients with a conversion disorder hitherto reported in a controlled neurophysiological investigation. Studies using evoked potentials have shown normal motor responses (Meyer *et al*., 1992) and early sensory components (Howard and Dorfman, 1986), but non-specific alteration in later components, such as P300 or CNV (Lorenz *et al*., 1998), consistent with normal processing in early neural pathways but changes in subsequent elaboration of response to stimuli. Only a few imaging studies using HMPAO-SPECT (Tiihonen *et al*., 1995; Yazici and Kostakoglu, 1998) or PET (Marshall *et al*., 1997; Spence *et al*., 2000) have been performed in patients with conversion symptoms, demonstrating inconstant abnormalities such as hyper- or hypoactivation in sensorimotor, parietal and/or frontal areas. These discrepancies may be due to a number of factors (e.g. small number of subjects, heterogeneous associated deficits or conditions of activation during scanning). A PET study (Marshall *et al*., 1997) performed in a single patient with long-lasting hysterical problems reported no activation of primary motor cortex when the patient attempted to move the affected leg (as can be expected given the lack of movement), together with an increased activity in right orbitofrontal and cingulate cortex that was interpreted as the source of active inhibition exerted on primary motor cortex. However, orbitofrontal and cingulate activity might also influence motor function through their inputs into basal ganglia and thalamic circuits (Graybiel *et al*., 1994; Kawagoe *et al*., 1998), or alternatively reflect monitoring of movement failure or motivational conflicts (Ebert and Ebmeier, 1996; Frith and Dolan, 1998; Fink *et al*., 1999). In two of our patients, we found increased activity in the right temporal pole (BA 38) during symptoms, possibly corresponding to limbic areas close to the amygdala and orbitofrontal cortex, but no such changes were observed in the remaining patients. Another recent PET study described reduced activation of left frontal regions in three patients with hysterical weakness of left limbs (Spence *et al*., 2000). However, in the absence of repeated measures after recovery, left frontal hypoactivity might also be related to antecedents of depression (Ebert and

Ebmeier, 1996; Elliott *et al*., 1997; Frith and Dolan, 1998), commonly observed in these patients (Marsden, 1986; Ron, 1994; Trimble, 1996). Test–retest designs are important to differentiate state from trait abnormalities in neuroimaging studies of complex psychiatric disorders (Ebert and Ebmeier, 1996; Frith and Dolan, 1998). In our patients, left frontal hypoactivity was inconstant but seen after recovery in three cases (BA 46 and/or 6). Several of our patients had depressed mood. Taken together, these findings may converge with other psychological, epidemiological and biological results (Merskey, 1995; Trimble, 1996; Tunca *et al*., 1996), suggesting a relationship between depressive disorders and conversion symptoms. Our results indicate that decreased activity in subcortical structures might be more directly related to the presence of contralateral conversion deficits themselves, rather than to other comorbid traits, which may coexist and outlast such transient deficits. It is also possible that abnormal striatal and thalamic activity might represent downstream effects due to primary dysfunction in orbitofrontal, cingulate or prefrontal cortex, allowing for the actual 'implementation' of motor inhibition associated with conversion symptoms.

These findings provide novel constraints for a modern psychobiological theory of hysteria. Given the role of striatal–thalamic circuits in many cognitive and affective domains (Alexander *et al*., 1986; Graybiel *et al*., 1994; Rauch and Savage, 1997), they also raise an intriguing question of whether similar mechanisms might participate in other non-motor hysterical disorders (e.g. memory). Future studies using newer techniques such as functional MRI are needed to extend these findings and explore other modalities of hysterical deficits. Functional connectivity analyses (e.g. Friston, 1994) might prove of particular interest in this context. Importantly, while hysterical disorders are usually defined by exclusion of an organic disease, the present findings of specific neurophysiological correlates may contribute to support a more positive diagnosis. In our recent clinical experience, this may help to reassure both patients and medical carers that hysterical symptoms are indeed functional, but nonetheless real, rather than mere imagination or malingering (Merskey, 1995). William James remarked long ago (James, 1896): 'Poor hysterics. First they were treated as victims of sexual trouble . . . then of moral perversity and mediocrity . . . then of imagination. Among the various rehabilitation which our age has seen, none are more deserving or humane. It is a real disease, but a mental disease.'

Acknowledgements

We wish to thank M. Allaoua, J. P. Papazyan, J. Billet, W. Pasini and A. Nahory for their support and helpful assistance, F. Vingerhoets for advice with SSM analysis, and R. Rafal, J. Kihlstrom, P. Halligan and R. Dolan for helpful comments and suggestions. P.V. was supported by a grant from the Swiss National Science Foundation. Part of this work was presented at the 51st Annual Meeting of the American Academy of Neurology, Toronto, April 1999, and at the European Meeting of Nuclear Medicine, Madrid, September 1999.

References

Alexander GE, Moeller JR. Application of the Scaled Subprofile Model to functional imaging in neuropsychiatric disorders: a principal component approach to modeling brain function in disease. Hum Brain Mapp 1994; 2: 79–94.

Alexander GE, DeLong MR, Strick PL. Parallel organization of functionally segregated circuits linking basal ganglia and cortex. [Review]. Annu Rev Neurosci 1986; 9: 357–81.

American Psychiatric Association. Diagnostic and statistical manual of mental disorders. DSM-IV. 4th ed. Washington (DC): Amercian Psychiatric Association; 1994.

Bhatia KP, Marsden CD. The behavioural and motor consequences of focal lesions of the basal ganglia in man. Brain 1994; 117: 859–76.

Billet J, Slosman DO. Improvement of quantification in SPECT using transmission computed tomography: utilisation of 153-GD transmission sources [abstract]. Eur J Nucl Med 1998; 25: 1141.

Binzer M, Kullgren G. Motor conversion disorder: a prospective 2- to 5-year follow-up study. Psychosomatics 1998; 39: 519–27.

Brown RG, Pluck G. Negative symptoms: the 'pathology' of motivation and goal-directed behaviour. [Review]. Trends Neurosci 2000; 23: 412–17.

Charcot JM. Leçons du mardi à la Salpêtrière: policlinique, 2nd ed. 1887–1888. Paris: Louis Battaille; 1892.

Chudler EH, Dong WK. The role of the basal ganglia in nociception and pain. [Review]. Pain 1995; 60: 3–38.

Coghill RC, Talbot JD, Evans AC, Meyer E, Gjedde A, Bushnell MC, et al. Distributed processing of pain and vibration by the human brain. J Neurosci 1994; 14: 4095–108.

de Ceballos ML, Baker M, Rose S, Jenner P, Marsden CD. Do enkephalins in basal ganglia mediate a physiological motor rest mechanism? Mov Disord 1986; 1: 223–33.

Eames P. Hysteria following brain injury. J Neurol Neurosurg Psychiatry 1992; 55: 1046–53.

Ebert D, Ebmeier KP. The role of the cingulate gyrus in depression: from functional anatomy to neurochemistry. [Review]. Biol Psychiatry 1996; 39: 1044–50.

Eidelberg D, Moeller JR, Ishikawa T, Dhawan V, Spetsieris P, Silversweig D, et al. Regional metabolic correlates of surgical outcome following unilateral pallidotomy for Parkinson's disease. Ann Neurol 1996; 39: 450–9.

Elliott R, Baker SC, Rogers RD, O'Leary DA, Paykel ES, Frith CD, et al. Prefrontal dysfunction in depressed patients performing a complex planning task: a study using positron emission tomography. Psychol Med 1997; 27: 931–42.

Ferbert A, Priori A, Rothwell JC, Day BL, Colebatch JG, Marsden CD. Interhemispheric inhibition of the human motor cortex. J Physiol (Lond) 1992; 453: 525–46.

Fink GR, Marshall JC, Halligan PW, Frith CD, Driver J, Frackowiak RS, et al. The neural consequences of conflict between intention and the senses. Brain 1999; 122: 497–512.

Flor-Henry P, Fromm-Auch D, Tapper M, Schopflocher D. A neuropsychological study of the stable syndrome of hysteria. Biol Psychiatry 1981; 16: 601–26.

Freud S, Breuer J. Studies on hysteria. New York: Basic Books; 1957.

Friston KJ. Functional and effective connectivity in neuroimaging: a synthesis. Hum Brain Mapp 1994; 2: 56–78.

Friston KJ, Holmes AP, Worsley KJ, Poline JB, Frith CD, Frackowiak RSJ. Statistical parametric maps in functional imaging: a general linear approach. Hum Brain Mapp 1995; 2: 189–210.

Frith C, Dolan RJ. Images of psychopathology. [Review]. Curr Opin Neurobiol 1998; 8: 259–62.

Gandevia SC. Roles for perceived voluntary motor commands in motor control. Trends Neurosci 1987; 10: 81–5.

Gold M, Adair JC, Jacobs DH, Heilman KM. Anosognosia for hemiplegia: an electrophysiologic investigation of the feed-forward hypothesis. Neurology 1994; 44: 1804–8.

Graybiel AM, Aosaki T, Flaherty AW, Kimura M. The basal ganglia and adaptive motor control. [Review]. Science 1994; 265: 1826–31.

Halligan PW, David AS. Conversion hysteria: towards a cognitive neuropsychological account. (Special issue of Cognitive Neuropsychiatry). Hove (UK): Psychology Press; 1999.

Hécaen H, Talairach J, David M, Dell MB. Coagulations limitée du thalamus dans les algies du syndrome thalamique: résultats thérapeutiques et physiologiques. Rev Neurol 1949; 81: 917–31.

Hellman RS, Tikofsky RS, Collier BD, Hoffmann RG, Palmer DW, Glatt SL, et al. Alzheimer disease: quantitative analysis of I-123-iodoamphetamine SPECT brain imaging. Radiology 1989; 172: 183–8.

Howard JE, Dorfman LJ. Evoked potentials in hysteria and malingering. J Clin Neurophysiol 1986; 3: 39–49.

Hui KK, Liu J, Makris N, Gollub RL, Chen AJ, Moore CI, et al. Acupuncture modulates the limbic system and subcortical gray structures of the human brain: evidence from fMRI studies in normal subjects. Hum Brain Mapp 2000; 9: 13–25.

Iadarola M, Max MB, Berman KF, Byas-Smith MG, Coghill RC, Gracely RH, et al. Unilateral decrease in thalamic activity observed with positron emission tomography in patients with chronic neuropathic pain. Pain 1995; 63: 55–64.

James W. On exceptional mental states: the 1896 Lowell lectures. New York: Charles Scriber's Sons; 1896.

Janet P. L'état mental des hystériques: les acidents mentaux. Paris: Rueff, 1894.

Kawagoe R, Takikawa Y, Hikosaka O. Expectation of reward modulates cognitive signals in the basal ganglia. Nat Neurosci 1998; 1: 411–6.

Kihlstrom JF. One hundred years of hysteria. In: Lynn SJ, Rhue JW, editors. Dissociation: clinical and theoretical perspectives. New York: Guilford Press; 1994. p. 365–94.

Kretschmer E. Hysteria: reflex and instinct. London: Peter Owen; 1960.

Lackner JR, Di Zio P. Some efferent and somatosensory influences on body orientation and oculomotor control. In: Spillmann L, Wooten BR, editors. Sensory experience, adaptation, and perception. Hillsdale (NJ): Lawrence Erlbaum; 1984. p. 281–301.

Laplane D, Baulac M, Carydakis C. Négligence motrice d'origine thalamique. Rev Neurolo (Paris) 1986; 142: 375–9.

Lorenz J, Kunze K, Bromm B. Differentiation of conversive sensory loss and malingering by P300 in a modified oddball task. Neuroreport 1998; 9: 187–91.

Ludwig AM. Hysteria: a neurobiological theory. Arch Gen Psychiatry 1972; 27: 771–7.

Marsden CD. Hysteria: a neurologist's view. Psychol Med 1986; 16: 277–88.

Marshall JC, Halligan PW, Fink GR, Wade DT, Frackowiak RS. The functional anatomy of a hysterical paralysis. Cognition 1997; 64: B1–8.

Merskey H. The analysis of hysteria: understanding conversion and dissociation. 2nd ed. London: Gaskell; 1995.

Meyer BU, Britton TC, Benecke R, Bischoff C, Machetanz J, Conrad B. Motor responses evoked by magnetic brain stimulation in psychogenic limb weakness: diagnostic value and limitations. J Neurol 1992; 239: 251–5.

Miller E. Hysteria: its nature and explanation. [Review]. Br J Clin Psychol 1987; 26: 163–73.

Mogenson GJ, Jones DL, Yim CY. From motivation to action: functional interface between the limbic system and the motor system. [Review]. Prog Neurobiol 1980; 14: 69–97.

Mountz JM, Bradley LA, Modell JG, Alexander RW, Triana-Alexander M, Aaron LA, et al. Fibromyalgia in women: abnormalities of regional cerebral blood flow in the thalamus and the caudate nucleus are associated with low pain threshold levels. Arthritis Rheum 1995; 38: 926–38.

Pawlik G. Statistical analysis of functional neuroimaging data: exploratory versus inferential methods. [Review]. J Cerebr Blood Flow Metab 1991; 11 Suppl. 1: A136–9.

Rauch SL, Savage CR. Neuroimaging and neuropsychology of the striatum: Bridging basic science and clinical practice. [Review]. Psychiatr Clin North Am 1997; 20: 741–68.

Rolls ET. A theory of emotion and consciousness, and its application to understanding the neural basis of emotion. In: Gazzaniga MS, editor. The cognitive neurosciences. Cambridge (MA): MIT Press; 1995. p. 1091–106.

Ron MA. Somatisation in neurological practice [editorial]. [Review]. J Neurol Neurosurg Psychiatry 1994; 57: 1161–4.

Rossini PM, Filippi MM, Vernieri F. Neurophysiology of sensori-motor integration in Parkinson's disease. [Review]. Clin Neurosci 1998; 5: 121–30.

Rougeul-Buser A, Bouyer JJ, Montaron MF, Buser P. Patterns of activities in the ventro-basal thalamus and somatic cortex SI during behavioral immobility in the awake cat: focal waking rhythms. In:

Massion J, Paillard J, Schultz W, Wiesendanger M, editors. Neural coding of motor performance. Experimental Brain Research, Suppl. 7. Berlin: Springer Verlag; 1983. p. 69–87.

Schultz W. The primate basal ganglia and the voluntary control of behaviour. J Conscious Stud 1999; 6: 31–45.

Seitz RJ, Roland PE. Vibratory stimulation increases and decreases the regional cerebral blood flow and oxidative metabolism: a positron emission tomography (PET) study. Acta Neurol Scand 1992; 86: 60–7.

Seyal M, Ro T, Rafal R. Increased sensitivity to ipsilateral cutaneous stimuli following transcranial magnetic stimulation of the parietal lobe. Ann Neurol 1995; 38: 264–7.

Shishido F, Uemara K, Inugami A, Ogawa T, Fujita H, Shimosegawa E et al. Discrepant 99mTc-ECD images of CBF in patients with subacute cerebral infarction. Ann Nucl Med 1995; 9: 161–6.

Spence SA, Crimlisk HL, Cope H, Ron MA, Grasby PM. Discrete neurophysiological correlates in prefrontal cortex during hysterical and feigned disorder of movement [letter]. Lancet 2000; 355: 1243–4.

Steriade M, Llinás RR. The functional states of the thalamus and the associated neuronal interplay. [Review]. Physiol Rev 1988; 68: 649–742.

Stern DB. Psychogenic somatic symptoms on the left side: Review and interpretation. In: Myslobodsky MS, editor. Hemisyndromes: psychobiology, neurology, psychiatry. New York: Academic Press; 1983. p. 415–45.

Strafella A, Ashby P, Munz M, Dostrovsky JO, Lozano AM, Lang AE. Inhibition of voluntary activity by thalamic stimulation in humans: relevance for the control of tremor. Mov Disord 1997; 12: 727–37.

Talairach J, Tournoux P. A co-planar stereotactic atlas of the human brain. Stuttgart: Thieme; 1988.

Tempel LW, Perlmutter JS. Abnormal vibration-induced cerebral blood flow responses in idiopathic dystonia. Brain 1990; 113: 691–707.

Tiihonen J, Kuikka J, Viinamäki H, Lehtonen J, Partanen J. Altered cerebral blood flow during hysterical paresthesia [letter]. Biol Psychiatry 1995; 37: 134–5.

Tracey I, Becerra L, Chang I, Breiter H, Jenkins L, Borsook D, et al. Noxious hot and cold stimulation produce common patterns of brain activation in humans: a functional magnetic resonance imaging study. Neurosci Lett 2000; 288: 159–62.

Trimble MR. Biological psychiatry. 2nd ed. Chichester (UK): John Wiley; 1996.

Tunca Z, Fidaner H, Cimilli C, Kaya N, Biber B, Yesil S, et al. Is conversion disorder biologically related with depression? A DST study. Biol Psychiatry 1996; 39: 216–9.

von Giesen HJ, Schlaug G, Steinmetz H, Benecke R, Freund HJ, Seitz RJ. Cerebral network underlying unilateral motor neglect: evidence from positron emission tomography. J Neurol Sci 1994; 125: 129–38.

Vuilleumier P. Anosognosia. In: Bogousslavsky J, Cummings JL, editors. Behavior and mood disorders in focal brain lesions. Cambridge: Cambridge University Press; 2000. p. 465–519.

Watson RT, Miller BD, Heilman KM. Non-sensory neglect. Ann Neurol 1978; 3: 505–8.

Yazici KM, Kostakoglu L. Cerebral blood flow changes in patients with conversion disorder. Psychiatry Res 1998; 83: 163–8.

Yousry TA, Schmid UD, Alkadhi H, Schmidt D, Peraud A, Buettner A, et al. Localization of the motor hand area to a knob on the precentral gyrus: a new landmark. Brain 1997; 120: 141–57.

Received November 8, 2000. Revised January 31, 2001.
Accepted February 8, 2001

Appendix I

Brief patient histories

Patient V.U.

Forty-year-old, right-handed woman who fled from Algeria during childhood, escaping a shooting where relatives were killed. Chronic neck pain with left arm irradiation for several years after a car accident with no injury, but no previous somatoform or psychiatry diagnosis. Left arm weakness and numbness 2 months after moving furnitures when being forced to move home to Switzerland. She could not raise and maintain the left arm outstretched, only slight and slow movements of fingers. Decreased sensation to light touch on the whole arm without radicular distribution.

Patient T.A.

Sixteen-year-old, right-handed woman, born in Portugal, in conflict with parents since they moved to Switzerland. Sexual assault from a cousin 2 years before. Transient gait disturbances after breaking-up with her boyfriend 1 year before, reported by relatives, but no previous somatoform or psychiatry diagnosis. Sudden paralysis of both legs, then unilateral left hemiparesis and anaesthesia following a conflict in school. Complete absence of spontaneous movement and lack of report of any sensory stimulation (touch, pain, position) on the left side of the body.

Patient V.A.

Fifty-one-year-old, right-handed woman, divorced, whose son died from heart disease 1 year prior to the study. Heaviness, weakness and loss of dexterity of right limbs after her new companion suffered myocardial infarction while wrongly suspected of abusing a teenager. No sensory complaints.

Patient B.R.

Twenty-one-year-old, right-handed woman, with history of misconduct at school during teenage, but no psychiatric diagnosis. Pain with complete anaesthesia and weakness of the right leg a few months after surgery for suspected appendicitis. Unable to walk, stand or raise the leg from the bed, give-away weakness, diffusely decreased sensation to touch on entire right lower limb, without specific distribution, no sensory loss on the abdomen. Abdominal CT scan, X-rays and echography of hip joints were normal.

Patient L.M.

Twenty-nine-year-old, right-handed woman, born in east Africa, precarious immigration condition since moving to Switzerland 8 years ago, currently about to lose employment. Inability to move left arm and leg, which can be raised from the bed but uplift cannot be maintained. Can move fingers and grasp, with sudden give-away weakness. Preserved sensation except for dysaesthesia to light touch on whole left hemibody, including trunk, with straight-cut demarcation on midline.

Patient R.O.

Thirty-six-year-old, right-handed woman, overworked from familial and professional duties. Fatigue and depression for 2 months, progressive weakness of left limbs with loss of dexterity and difficulty walking. Slightly decreased sensation of left touch on left limbs and left trunk, with patchy distribution on limbs and trunk.

Patient L.A.

Fifty-four-year-old, left-handed man, depressed mood, conflict at work due to younger employees taking over. Back pain after a benign fall without loss of consciousness, then diffuse weakness of right hemibody, inability to move arm or leg except for brief uncoordinated jerky attempts. Patchy decreases of tactile sensation on right limbs.