Functional neuroanatomical correlates of hysterical sensorimotor loss

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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 99mTc-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 striatotegmental 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; T1 = vibratory stimulation with symptoms present; T2 = 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 neuro-
biological 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 neuropsychological
abnormalities (e.g. Tihonen 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,

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 proprio-
ceptive 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,
promotor 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
clean 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 dysesthesia (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; carotid-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 (T1 scan, seven cases) a few days later (2–4 days, mean 2.8); and during the same stimulation after recovery from deficit (T2 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 T2 scan. In T1 and T2 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 (99mTc-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 T1 and T2, 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 153Gd 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 153Gd 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)
There were two planned comparisons of interest: (i) activation comparisons to identify significant differences between 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-values were transformed to the unit normal distribution SPM(Z) with Z scores \( Z > 3.09 \) (uncorrected for multiple comparisons) to identify significant changes between conditions, and only activation foci with corrected significance of \( P < 0.01 \) at the cluster level were reported. There were two planned comparisons of interest: (i) activation during T1 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 T2 scan (symptoms recovered) versus activation during T1 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 (T2 versus T1) 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 \( P \leq 0.01 \); all reported comparisons correspond to \( P \leq 0.002 \) uncorrected using t-tests, \( P < 0.01 \) 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 \[ \% = \frac{(\text{contralateral} - \text{ipsilateral})}{(\text{contralateral} + \text{ipsilateral})} \times 200 \], and change percentages were computed using count differences between T1 and T2 scans in homologous ROIs for each hemisphere \[ \% = \frac{(T_2 - T_1)}{(T_2 + T_1)} \times 200 \].

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 \( \times \) 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 T1 and T2 data from all AOIs of the two hemispheres, in the four subjects who recovered, entered into the analysis without any \textit{a priori} specification about the possible relevant conditions (i.e. before or after recovery, contralateral or ipsilateral side). After all region \( \times \) 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 \( \times \) region
Table 1 Coordinates and magnitude of maximal rCBF changes in SPM analysis

<table>
<thead>
<tr>
<th>Brain side</th>
<th>Brodmann area</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>Z-score</th>
</tr>
</thead>
<tbody>
<tr>
<td>rCBF changes associated with bilateral vibrotactile stimulation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1 &gt; B</td>
<td>Contra Middle prefrontal gyrus (BA 6)</td>
<td>-34</td>
<td>14</td>
<td>52</td>
<td>4.27</td>
</tr>
<tr>
<td>T1 &gt; B</td>
<td>Contra Middle prefrontal gyrus (BA 8)</td>
<td>-32</td>
<td>50</td>
<td>0</td>
<td>3.28</td>
</tr>
<tr>
<td>T1 &gt; B</td>
<td>Contra Middle prefrontal gyrus (BA 8)</td>
<td>-32</td>
<td>34</td>
<td>38</td>
<td>3.15</td>
</tr>
<tr>
<td>T1 &gt; B</td>
<td>Contra Superior prefrontal gyrus (BA 9/46)</td>
<td>-26</td>
<td>46</td>
<td>28</td>
<td>2.99</td>
</tr>
<tr>
<td>T1 &gt; B</td>
<td>Contra Post-central gyrus (BA 5/2)</td>
<td>-34</td>
<td>-26</td>
<td>46</td>
<td>4.19</td>
</tr>
<tr>
<td>T1 &gt; B</td>
<td>Contra Post-central gyrus (BA 5)</td>
<td>-8</td>
<td>40</td>
<td>60</td>
<td>3.50</td>
</tr>
<tr>
<td>T1 &gt; B</td>
<td>Contra Superior parietal lobule (BA 7)</td>
<td>-22</td>
<td>-42</td>
<td>58</td>
<td>3.14</td>
</tr>
<tr>
<td>T1 &gt; B</td>
<td>Ipsi Superior prefrontal gyrus (BA 9/46)</td>
<td>40</td>
<td>28</td>
<td>36</td>
<td>3.85</td>
</tr>
<tr>
<td>T1 &gt; B</td>
<td>Ipsi Middle prefrontal gyrus (BA 46)</td>
<td>36</td>
<td>44</td>
<td>16</td>
<td>3.85</td>
</tr>
<tr>
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<td>Ipsi Superior prefrontal gyrus (BA 9)</td>
<td>22</td>
<td>50</td>
<td>52</td>
<td>3.36</td>
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<tr>
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<td>Ipsi Superior prefrontal gyrus (BA 8)</td>
<td>0</td>
<td>30</td>
<td>58</td>
<td>3.34</td>
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<td>16</td>
<td>-32</td>
<td>56</td>
<td>3.13</td>
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<tr>
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<td>Ipsi Post-central gyrus (BA 1/2)</td>
<td>28</td>
<td>-32</td>
<td>48</td>
<td>3.03</td>
</tr>
<tr>
<td>T1 &gt; B</td>
<td>B/Contra Cuneus/medial occipital gyrus (BA 19/18)</td>
<td>-18</td>
<td>-98</td>
<td>14</td>
<td>4.27</td>
</tr>
<tr>
<td>T1 &gt; B</td>
<td>Ipsi Inferior occipital gyrus (BA 18)</td>
<td>26</td>
<td>-86</td>
<td>-2</td>
<td>4.17</td>
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<td>22</td>
<td>-74</td>
<td>4</td>
<td>4.10</td>
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<tr>
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<td>Contra Inferior occipital gyrus (BA 18/19)</td>
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<td>-80</td>
<td>-8</td>
<td>3.25</td>
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<tr>
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<td>Ipsi Lingual gyrus (BA 18)</td>
<td>4</td>
<td>-76</td>
<td>-6</td>
<td>3.24</td>
</tr>
</tbody>
</table>

B = baseline resting state with symptoms present; T1 = vibratory stimulation with symptoms present; T2 = 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.

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 (T1) 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 (T1), rCBF during vibration was decreased in the contralateral thalamus and basal ganglia (caudate and putamen) compared with when the deficit was resolved (T2), while it was increased in the ipsilateral somatosensory (BA 1/3) and premotor (BA 6) 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.
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 (T₁), resolving after recovery (T₂). (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.
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 T1 and T2 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 T1. The second factor also reflects a network of prefrontal and parietal areas, loading more on the ipsilateral hemisphere during scan T1. 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 T1.

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 (T1), 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 ≥ 3.06, P < 0.005 in each case, Wilcoxon paired rank test) and contralateral caudate (~6 to ~30%, mean 15.9; Z ≥ 2.81, P < 0.005), together with a relative hyperactivation of the contralateral lenticular nucleus (+9 to +11%, mean 9.9; Z ≥ 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 ≥ 2.52, P < 0.01).

None of these asymmetries were seen after recovery (T2). Compared with T1, average normalized perfusion on T2 scans significantly increased for each patient in contralateral thalamus (+7 to +23%, mean 18%; Z ≥ 3.07, P < 0.005 in each case) and contralateral caudate (+12 to +36%, mean 22%; Z ≥ 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 ≥ 2.58, P < 0.01) and ipsilaterally (Z ≥ 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 ≥ 2.66, P < 0.01) contralateral to the deficit in two patients (V.U. and T.A.) and ipsilaterally 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 ≥ 2.66, P < 0.01), whereas no such asymmetry was noted during symptoms. No other asymmetries or changes were remarkable.

### Table 2 Topographical profiles in SSM analysis

<table>
<thead>
<tr>
<th></th>
<th>Factor 1</th>
<th>Factor 2</th>
<th>Factor 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eigenvalue</td>
<td>5.46</td>
<td>2.24</td>
<td>2.14</td>
</tr>
<tr>
<td>% variance explained</td>
<td>45.5</td>
<td>18.6</td>
<td>17.9</td>
</tr>
</tbody>
</table>

#### (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 |
| BA 46 | -0.75 |
| 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 |
| BA 37 | -0.53 |
| BA 17–18–19 | -0.72 |
| BA 22 | -0.75 |
| BA 20–21 | -0.55 |
| BA 38 | -0.82 |
| Caudate | 0.68 |
| Lenticular | -0.92 |
| Thalamus | 0.72 |

#### (B) Hemisphere (mean across subjects)

<table>
<thead>
<tr>
<th>T1-contralateral</th>
<th>T1-ipsilateral</th>
<th>T2-contralateral</th>
<th>T2-ipsilateral</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.43</td>
<td>0.59</td>
<td>0.77</td>
<td>0.80</td>
</tr>
<tr>
<td>-0.06</td>
<td>0.37</td>
<td>-0.07</td>
<td>-0.11</td>
</tr>
<tr>
<td>0.58</td>
<td>0.21</td>
<td>-0.24</td>
<td>-0.26</td>
</tr>
</tbody>
</table>

Factors indicate overlapping functional networks of brain areas whose activity is covarying across subjects and scan sessions (T1 and T2 = 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.
**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 T₁ 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 ± 0.034), while activity in the contralateral thalamus AOI was 2.39; Mann–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 (T₁), regressing with recovery (T₂). 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 T₁ and T₂ 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 (T₁–B), but decreased ipsilaterally more than contralaterally with recovery (T₁–T₂), 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 striatothalamocircuit 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 striatothalamocircuits 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 striatotanglumocortical circuits has been implicated in motor or cognitive inhibition associated with several neurological or psychiatric disorders, such as apathy and limbic inputs (Bhatia and Marsden, 1994; Rauch and Savage, 1997; Brown and Pluck, 2000). In animals, alert states with inhibition of volitional behaviour (Rougeul-Busset 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 dysesthesia or hypesthesia. 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


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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.