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Differential brain activations during intentionally simulated and subjectively experienced paralysis

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Introduction. Distinguishing conversion disorder from malingering presents a significant challenge as the diagnosis ultimately depends on the patient's subjective report and the clinician's suspicion of an intention to deceive. Using hypnosis to manipulate the intentionality of movement inhibition in the same subjects, we used positron emission tomography (PET) to determine whether failure to move during intentionally simulated and subjectively experienced paralysis is mediated by different neural structures.

Methods. Using a within-subject design, 12 normal, hypnotised subjects were tested under two paralysis conditions during the same scanning session. Half of the scans were performed with the suggestion that the left leg was paralysed (subjectively experienced paralysis condition) and half with the leg normal but with the instruction that paralysis should be feigned (intentionally simulated paralysis condition).

Results. Relative increases in brain activation were seen in the right orbitofrontal cortex, right cerebellum, left thalamus, and left putamen during subjectively experienced paralysis compared to intentionally simulated paralysis, although a previously reported activation of the right anterior cingulate cortex was not seen. During intentionally simulated paralysis compared to subjectively experienced paralysis relative increases in brain activation were seen in the left ventrolateral prefrontal cortex, and a number of right posterior cortical structures.

Conclusions. Our results suggest that subjectively experienced paralysis has a different neural basis to intentionally simulated paralysis. These findings have theoretical and clinical implications for malingering and related attempts to unravel the neuropsychological basis for conversion hysteria.

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Growing numbers of patients report a variety of neurological symptoms for which there appears to be no underlying biomedical cause (Carson et al., 2000; Ron, 1994). A significant proportion of these symptoms are thought to be psychologically mediated and hence beyond the influence or control of the patient. However, distinguishing subjectively experienced symptoms (historically described as hysterical or conversion disorder symptoms) from similar complaints in which subjects choose to intentionally simulate symptoms for personal gain (malingering) remains a difficult and sensitive clinical judgement. One key element of this conceptual distinction is that the subject who engages in malingering, unlike the patient with conversion disorder, is by definition considered to do so intentionally with deception as a means to secure personal benefit. In the case of motor paralysis, the clinical presentation for malingering and those experiencing conversion disorder can be clinically indistinguishable (i.e., both report that they cannot move the affected limb), but it is not clear whether different psychophysiological mechanisms mediate these conceptually distinct conditions. Since functional magnetic resonance imaging (MRI) of the brain provides a means of identifying brain changes accompanying the patient's subjective report, it offers an opportunity to explore the existence of different neural mechanisms underlying these qualitatively different mental states. This cognitive neuroscience approach has been employed previously with some success. A patient diagnosed with hysterical paralysis demonstrated that failure to move the affected (left) leg compared to the unaffected leg was associated with relatively increased activation in right anterior cingulate cortex extending into orbitofrontal cortex using positron emission tomography (PET) (Marshall, Halligan, Fink, & Frackowiak, 1997). Similar results were obtained in a subject with hypnotically suggested paralysis (Halligan, Athwal, Oakley, & Frackowiak, 2000). Both subjects reported the subjective experience of weakness in the affected limb in studies where there was no obvious intention or necessity to simulate their symptoms. Others have addressed the critical question of whether intentionally simulated symptoms have a different neural basis from subjectively experienced symptoms and have reported differential patterns of activation between three patients with weakness due to conversion hysteria compared to two subjects requested to intentionally simulate poor motor performance (Spence, Crimlisk, Cope, Ron, & Grasby, 2000). Our previous studies (Halligan et al., 2000; Marshall et al., 1997) and those of others (Raz & Shapiro, 2002), suggest that hypnosis is a particularly effective way to generate a compelling experience of subjective paralysis. Comparing intentionally simulated paralysis in the same hypnotised subjects with a hypnotically suggested (subjectively experienced) paralysis, as we have done in the present study, strategically controls for the effects of hypnosis *per se* and provides a powerful means when used in conjunction with functional imaging to demonstrate the different neural mechanisms underling behaviourally indistinguishable symptom presentations. The aim of this study was to test the hypothesis that the failure to move during

feigned (intentionally simulated) and hypnotically suggested (subjectively experienced) paralysis would be mediated by different neural networks.

MATERIALS AND METHODS

Subjects

A total of 12 healthy male student volunteers (age range 18–21 years, mean 19.8 years) were preselected for scoring at least 8 (out of 12) on the Harvard Group Scale of Hypnotic Susceptibility (HGSHS; Shor & Orne, 1962), with positive scores on all items dealing with ideomotor responses, motor rigidity, and inhibition of movement (mean HGSHS score 9.5 ± 0.71) and via an individual screening procedure. This screening test involved the hypnotic induction, deepening and ''special place'' procedures followed by suggestions of left leg paralysis that were to be used in the main study (see below). Participants were accepted into the study if they reported a subjectively convincing involuntary paralysis and showed no overt movement of the leg when instructed to try to move it following the paralysis suggestions. Participants showing no left leg movement in the paralysis condition used 100 mm Visual Analogue Scales to rate the involuntariness of their paralysis (0 = completely voluntary: ''I didn't try to move it but could have''; 100 = completely involuntary: ''I tried to move it but couldn't''). The mean rating of involuntariness for the 12 subjects reported here was 86.83 (*SD* ± 14.81). All moved their right legs normally during left leg paralysis when asked to do so. There are no obvious order effects in the subjective data concerning the involuntariness of the hypnotic paralysis—for example, when the paralysis was experienced first the mean perceived involuntariness was 81.83 (*SD* ± 14.46) and when it was experienced second 81.00 (*SD* ± 15.4).

All subjects were right-handed according to the Edinburgh handedness scale (Oldfield, 1971). They reported no history of neurological illness or psychiatric history and were not taking regular medication. Full written consent was obtained from all subjects in accordance with the Declaration of Helsinki. The study was approved by the Joint Ethics Committee of the Institute of Neurology and National Hospital for Neurology and Neurosurgery, London, and permission to administer radioactive $H_2[^{15}O]$ was given by the Administration of Radioactive Substances Advisory Committee of the Department of Health, UK.

Hypnosis procedures

An eyes-closed hypnotic induction was carried out before scanning commenced, with relaxation suggestions and deepening, involving ''descent'' and ''special place'' imagery (Heap & Aravind, 2002). Two paralysis conditions were employed, both during hypnosis: (1) suggested flaccid paralysis of the left leg (subjectively experienced paralysis); and (2) normal left leg, but with an

instruction to feign the same paralysis (intentionally simulated paralysis). The key elements of the leg paralysis suggestion were: ''The muscles of your left leg becoming floppy, relaxed and unable to move . . . paralysed and quite unable to move . . . with the sensation of touch remaining normal . . . the muscles becoming out of touch with your thoughts wishes and intentions . . . so that even if you try to move the muscles fail to respond in any way''. At the end of the subjectively experienced paralysis condition the experience of paralysis was removed by reversing these suggestions. In the intentionally simulated paralysis condition no paralysis suggestions were given and the same subjects were instructed that, although their left leg was ''completely normal and able to move'', they were to feign (i.e., pretend) a similar leg paralysis to deceive an observer together with a small financial incentive (10 pounds sterling) available if successful in doing so. Participants remained hypnotised in the subjectively experienced paralysis-to-simulated paralysis condition while the paralysis suggestion was removed. They were then asked to move their legs and to indicate when both legs felt the same and were equally easy to move before continuing with the session. In the simulated paralysis-to-subjectively experienced paralysis condition a comparable amount of time was spent midway in introducing the paralysis and checking that the suggestion had produced the desired effect.

Hypnotic depth (the continuation of an ''as real'' special place experience) and the presence (or absence as appropriate) of the subjective experience of the paralysis were checked throughout the scanning session by employing voluntary finger signals. The mean overall duration of hypnosis (from initial eye closure to eye-opening during termination of the hypnosis procedure) was 131.27 minutes (*SD* ± 10.72). There were no indications from retrospective subjective reports or from our own observations that participants found it difficult to maintain the hypnosis condition for that length of time. The participants own estimation of the length of the hypnosis session was 76.67 minutes: *SD* ± 35.25 (i.e., slightly over half its actual length: 58.25%), suggesting that they were absorbed in the experience, which they described as as relaxing and enjoyable.

Experimental design

Within each of the paralysis conditions two types of scan were employed for all 12 subjects: ''rest'' (A, no movement) and ''active'' (B). The two paralysis conditions were run in separate blocks in a randomised counterbalanced order. During the active scans, subjects were asked by the observer, who was blind to the paralysis condition, to attempt to lift their left leg in synchrony with a metronome tone (0.5 Hz). During rest scans the metronome was sounded but no response was required. Scanning was performed in two blocks of six scans, carried out in the order ABABAB. Each block was performed during either paralysis condition 1: subjectively experienced paralysis (A1, B1), or paralysis condition 2: intentionally simulated paralysis (A2, B2), in a randomised

counterbalanced order. Before hypnotic induction, neurological examination was entirely normal for all subjects.

Direct observation of the subjects was used to record any visible limb movements made during scanning. Subjects were made aware that they were being observed continually by the experimenters and by an observer, who also conducted a neurological examination of each subject's legs and lower body halfway through each of the two paralysis conditions. This observer, an experienced neurologist, was not informed as to the order of the two paralysis conditions for any given subject. In addition, to monitor the possibility of sustained muscle contraction without movement, surface electromyogram (EMG) recordings were made. Standard EMG leads were taped to the skin overlying quadriceps femoris and biceps femoris muscles at the point of maximum palpable contraction in both legs. The EMG signal was fed into a signal conditioner (CED 1902, Cambridge Electronic Design, Cambridge, UK). This signal was digitised (CED 1401, Cambridge Electronic Design, Cambridge, UK) and fed into a computer running Spike 2 (Cambridge Electronic Design, Cambridge, UK). A significant muscle contraction was taken as that generating a peak deflection of amplitude >5% of the peak amplitude obtained during prescan testing. All subjects were asked by the informed experimenter in a debriefing session immediately after the scanning was complete to rate the ''voluntariness'' of their ''paralysis'' in each of the two paralysis conditions on a 100 mm visual analogue scale (where 0 = ''completely voluntary—I could have moved my leg easily'' and 100 = ''completely involuntary—I could not move my leg'').

Data acquisition

The subjects lay supine in the scanner. Head movement was reduced by a padded helmet with chinstrap, fixed to the headrest. PET was performed using a CTI ECAT HR plus scanner (CTI, Knoxville, TN, USA) in three-dimensional mode with interdetector collimating septa removed. The axial field of view was 155 mm providing whole brain coverage including cerebellum. Regional cerebral blood flow (rCBF) was measured using $H_2[^{15}O]$. Background activity was counted over 30 seconds prior to each image and 6–10 milliCuries (mean 8.9 mCi) were delivered over 20 seconds to the right arm. Image acquisition began 5 seconds before the rising phase of the count curve, approximately 25 seconds after injection, and continued for 90 seconds. Correction for tissue and helmet attenuation was made using a transmission scan from 68 Ga/68 Ge sources at the start of the scanning session. The interscan interval was 9 minutes. Corrected data were reconstructed by three-dimensional filtered back-projection (Hanning filter, cut-off frequency 0.5 cycles/pixel) and scatter correction. Sixty-three transverse planes were obtained with 128 × 128 pixel image matrix, with a resulting pixel size of 2.4 × 2.1 × 2.1 mm, and a resolution of 6 mm at full width half maximum.

Anatomic structural images were acquired for all subjects on the same day, using a VISION MR scanner at 2 tesla (Siemens, Erlangen, Germany) with a T1 MPRAGE sequence (TE = 4 ms, TR = 9.5 s, TI = 600 ms, resolution 1 × 1 × 1.5 mm, 108 axial slices).

Image analysis

All analyses of images were made using Statistical Parametric Mapping software, SPM99 (Wellcome Department of Imaging Neuroscience, London, UK; http://www.fil.ion.ucl.ac.uk/spm), in the MATLAB 5 environment (Mathworks, Sherborn, MA). Images were realigned to the first image by rigid body correction for head movements between scans (Friston et al., 1995 a and b). All images were normalised to a standardised anatomic space, by matching each image to a standardised template using linear and nonlinear spatial transformations (Holmes et al., 1998). Each image was smoothed with a 12 mm isotropic full width half maximum gaussian kernel to account for intersubject differences in anatomy and to allow valid statistical inference according to gaussian random field theory.

Statistical analysis was performed using a multisubject single group fixed-effects model, in which each of the four conditions (A1, B1, A2, B2) were modelled as separate covariates across the group. In addition, the effect of global differences in cerebral blood flow between scans was modelled as a covariate of no interest by subject-specific ANCOVA scaling of activity to a nominal mean global activity of 50 ml/100 g/min (Friston et al., 1990). The resulting covariates were used in a general linear model (Price & Friston, 1997). The parameter estimates for each covariate resulting from the least mean squares fit of the model to the data were calculated and statistical parametric maps of the *t*-statistic (SPM{*t*}) resulting from linear contrasts of covariates were generated and stored as separate images. In this way: we generated SPM{*t*}s representing: (1) the main effects of active (B) compared to rest (A) for each paralysis condition ([B1-A1] and [B2-A2]); and (2) differential task-related activations between the two paralysis conditions ([B1-A1]–[B2-A2] and [B2-A2]–[B1-A1]). In addition, we performed a conjunction analysis between the two main effects ([B1-A1] and [B2-A2]) in order to determine shared task-related activations between the two paralysis conditions. Conjunction analysis relies on the conjoint testing of multiple, in this case two, effects such that the null hypotheses that there is no effect of the ''attempt to move'' instruction during subjectively experienced paralysis, and no effect of the same instruction during intentionally simulated paralysis, can be jointly rejected (Price & Friston, 1997).

All SPM{*t*}s were transformed to the unit normal *Z*-distribution to create a statistical parametric map (SPM{*Z*}). All *t*-tests carried out within SPM were one-tailed. Anatomical identification was carefully performed by superimposing the maxima of activation foci both on the Montreal Neurological Institute (MNI)

reference brain and on the normalised structural images of each subject, and labelling with the aid of the atlas of Duvernoy (1991).

RESULTS

Behavioural results

Direct observation throughout scanning revealed no discernible movements of the relevant limbs for any subject. In addition, no significant muscle activity was demonstrated with surface EMG during any condition in any subject. The mean voluntariness rating during the intentionally simulated paralysis condition was 18.25 (*SD* = 11.39: range 3–36) and during the subjectively experienced paralysis condition it was 81.42 (*SD* = 14.26: 54–97). All subjects described being conscious of the need to convince the uninformed observer of their ''paralysis'' throughout the intentionally simulated paralysis condition. Some subjects reported being aware from their experience in the current session or from prescanning screening of changes, such as slight alterations in breathing or facial expression, during attempted leg movements in the subjectively experienced limb paralysis condition and had intentionally produced these signs also in the simulated paralysis condition. There were no differences in the clinical presentations of the hypnotic paralysis and the feigning conditions that enabled the uninformed observer to distinguish between them at above chance level. On the 12 occasions it was examined by the neurologist/observer (once for each participant) simulated paralysis was correctly identified four times (33.33%), incorrectly identified as subjectively experienced on three occasions, and on five occasions no identification was made. For subjectively experienced paralysis the corresponding figures are: correct 2 times (16.67%); incorrect 2 times; and no identification 8 times. Overall, of 24 observations there were 6 correct identifications (25%), 5 incorrect identifications, and 13 undecided. Overall these observations clearly indicate that the behavioural presentations of the two paralysis conditions were clinically indistinguishable so that on most occasions there was not enough evidence to form an opinion and on those occasions where a judgement was offered it was at no more than chance level.

The neurologist's reports are consistent with both paralysis conditions corresponding more closely in presentation to conversion disorder paralysis than a physically produced (neurological) paralysis. It was anticipated that the memory of the subjectively experienced paralysis might help participants to simulate the same paralysis when the simulation condition came second. There was no evidence that this happened, however. In the simulate-first group the neurologist misidentified the simulated paralysis as a subjectively experienced paralysis on two occasions. In the simulate-second group (where simulation should have been made more convincing by the previous experience of paralysis) only one simulated paralysis was misidentified as subjectively experienced. Equally, the order of the two conditions had no effect on the participants' confidence in how

successful they felt they had been in deceiving the observer that their simulated paralysis was a subjectively experienced paralysis. In the simulate-first group the confidence rating was 50.83% (*SD* ± 21.19) and 50.16% (*SD* ± 23.78) in the paralysis-first group.

Imaging results: Main effects of attempted movement

Attempted movement during subjectively experienced paralysis compared to rest, led to relatively increased activation in the bilateral putamen, left thalamus, left supplementary motor area (SMA), left cerebellum, and right posterior medial orbitofrontal cortex (Figure 1A and Table 1). Feigning attempted movement during intentionally simulated paralysis compared to rest led to relatively increased activation in a different set of regions, including the left

TABLE 1
Voxels which are significantly activated during attempted movement compared to rest

	Talairach coordinates in MNI space			
Region	*x*	*y*	*z*	*Z-value*
(a) During perceived paralysis				
R putamen	28	−2	6	5.73
L putamen	−18	−6	8	5.33
L thalamus (mediodorsal)	−4	−20	8	4.85
R orbitofrontal cortex	18	12	−14	4.58
L cerebellum	−22	−48	−40	4.63
L SMA	−2	−12	64	4.15*
(b) During feigning				
R parietal operculum (S II)	50	−28	24	5.71
L inferior frontal sulcus	−36	34	24	5.27
R SMA	6	−18	62	5.27
R ventral premotor cortex	52	6	8	5.17
L cerebellum	−32	−52	−36	5.06
R cerebellum	26	−44	−38	4.83
L inferior parietal cortex	−44	−54	46	4.77

[a] x, distance (mm) to right (+) or left (−) of midsaggital line; y, distance anterior (+) or posterior (−) to vertical plane through the anterior commissure; z, distance above (+) or below (−) the intercommissural (AC-PC) line. The AC-PC line is the horizontal line between the anterior and posterior commissures. All voxels are significant at $p < .05$ (corrected for multiple comparisons across whole brain). * Represents the peak voxel in a cluster significant at $p < .05$ (corrected for multiple comparisons across whole brain).

R = right; L = left; SMA = supplementary motor area; AC = anterior commissure; PC = posterior commissure.

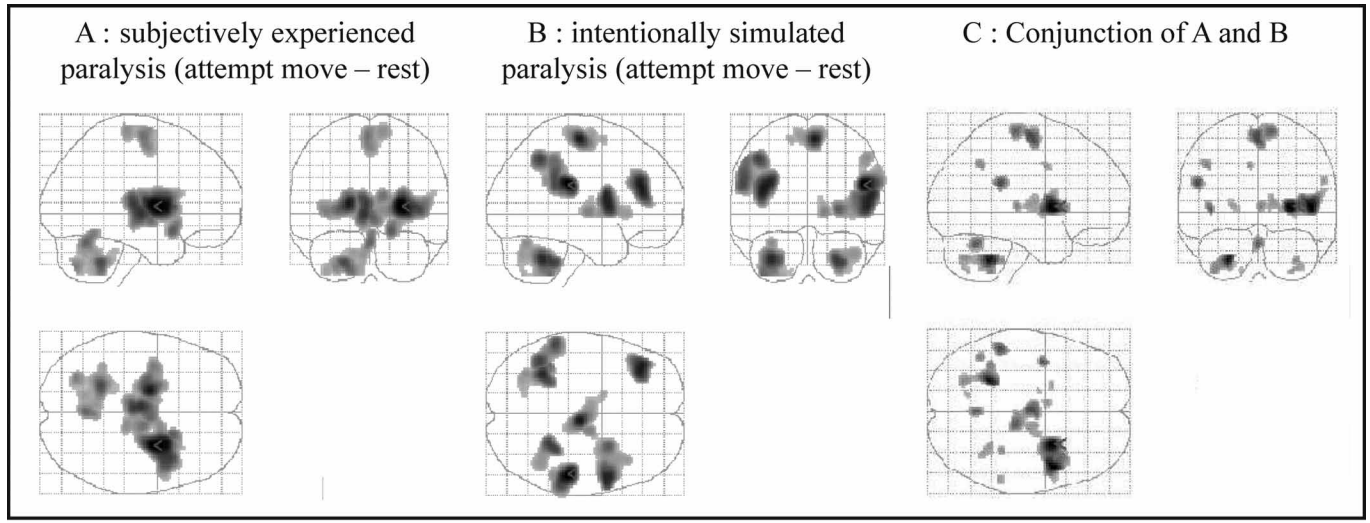

Figure 1. SPM{*Z*}s representing the categorical comparison of brain activations following the instruction to attempt to move the left leg compared to rest during (A) subjectively experienced paralysis (B1-A1), and (B) intentionally simulated paralysis (B2-A2), and (C) the conjunction of the main effects (B1-A1) and (B2-A2). The SPM{*Z*}s are shown as maximum intensity projections. The brain is shown from the right, top, and back. Results for (A) and (B) are shown at cluster level significance (clusters are significant at $p < .05$, corrected for multiple comparisons across whole brain) for display purposes. All voxels in (C) are significant at $p < .05$, corrected for multiple comparisons across whole brain.

prefrontal cortex, left inferior parietal cortex, right parietal operculum, right SMA, right ventral premotor cortex, and bilateral cerebellar hemispheres (Figure 1B and Table 1). The cluster of voxels in the left prefrontal cortex was centred on the inferior frontal sulcus, and therefore it was not possible to categorise as the dorsolateral (DLPFC) or ventrolateral prefrontal cortex (VLPFC).

Conjunction analysis of these main effects demonstrated relatively increased activation in a number of regions bilaterally, although more strongly in the right hemisphere (Figure 1C and Table 2). In particular, ''attempt to move'' related activations were seen in the bilateral SMA, insula, and inferior parietal cortex, as well as in the bilateral putamen, and cerebellar hemispheres during both paralysis conditions. Lateralised increases were also noted in the right thalamus, and left anterior cingulate gyrus. Attempted movement during subjectively experienced paralysis compared to rest, led to relatively decreased activation in the right middle occipital gyrus ($x = 48$, $y = -68$, $z = 24$, Z-value = 5.13, $p = .004$, corrected for multiple comparisons across the whole brain) only. At the same threshold, there were no relative decreases in activation with the same instructions to attempt to move during intentionally simulated paralysis compared to rest.

TABLE 2
Voxels for which the conjunction of main effects of active compared to rest for either subjectively experienced paralysis (B1-A1) or intentionally simulated paralysis (B2-A2) are significant[a]

	Talairach coordinates in MNI space			
Region	*x*	*y*	*z*	*Z-value*
L SMA	−2	−12	62	5.83
R SMA	10	−26	66	5.62
L inferior parietal	−52	−38	24	5.83
	−44	−56	40	5.27
R inferior parietal	56	−40	26	5.09
L insula	−40	−2	2	5.61
R insula	46	6	4	6.59
L cingulate gyrus	−8	8	38	5.08
L cerebellum	−26	−48	−40	6.37
R cerebellum	32	−50	−46	5.04
Cerebellar vermis	0	−58	−26	5.63
L putamen	−22	6	6	5.03
R putamen	28	6	4	6.53
R thalamus (ventomedial)	12	−14	6	5.09

[a] All voxels are significant at $p < .05$ (corrected for multiple comparisons across whole brain).

L = left; R = right; SMA = supplementary motor area.

Imaging results: Task related differential activations

During subjectively experienced paralysis compared to intentionally simulated paralysis, increased activation was seen in the right posterior medial orbitofrontal cortex (Figure 2A), left putamen and thalamus, and right cerebellum (Table 3). During intentionally simulated paralysis compared to subjectively experienced paralysis, activation was seen in the left ventrolateral prefrontal cortex (BA45) (Figure 2B), as well as in the right medial parietal cortex, intraparietal sulcus, parietal operculum, and superior temporal sulcus (Table 3).

The comparison ([B2-A2]–[B1-A1]) identifies voxels in which there is a relative increase in activation when feigning attempted movement compared to rest during the intentionally simulated paralysis condition, or a relative decrease in activation with attempted movement compared to rest during subjectively experienced paralysis. The converse is true for the comparison ([B1-A1]–[B2-A2]). The relative contributions of each of these components can be judged only by plotting the parameter estimates for each condition at the voxel of interest. A

TABLE 3

Peak voxels resulting from the comparison of increases in rCBF following the instruction to attempt to move the left leg during (A) subjectively experienced paralysis compared to intentionally simulated paralysis ([B1-A1] − [B2-A2]), and (B) intentionally simulated paralysis compared to subjectively experienced paralysis ([B2-A2] − [B1-A1])[a]

	Talairach coordinates in MNI space			
Region	*x*	*y*	*z*	*Z-value*
A. Paralysis compared to feigning				
R orbitofrontal cortex	18	12	−16	3.72
R cerebellum	12	−54	−50	3.56
L thalamus (mediodorsal)	−30	2	−4	3.35
L putamen	−4	−10	2	3.32
B. Feigning compared to paralysis				
L VLPFC (BA 45)*	−46	34	14	3.81
R parietal operculum	48	−28	28	3.64
R posterior superior temporal sulcus	54	−54	6	3.47
R intraparietal sulcus	28	−50	38	3.46
R medial parietal cortex	2	−58	54	3.29

[a] All voxels are significant at $p < .001$ (uncorrected for multiple comparisons across whole brain).

* The corrected *p*-value for the activation at left ventrolateral prefrontal cortex is $p = .025$, based on a small volume correction using a search volume of 20 mm radius centred at $x = -48$, $y = 36$, $z = 28$, based on previously published work (Spence et al., 2000).

L = left; R = right; VLPFC = ventrolateral prefrontal cortex.

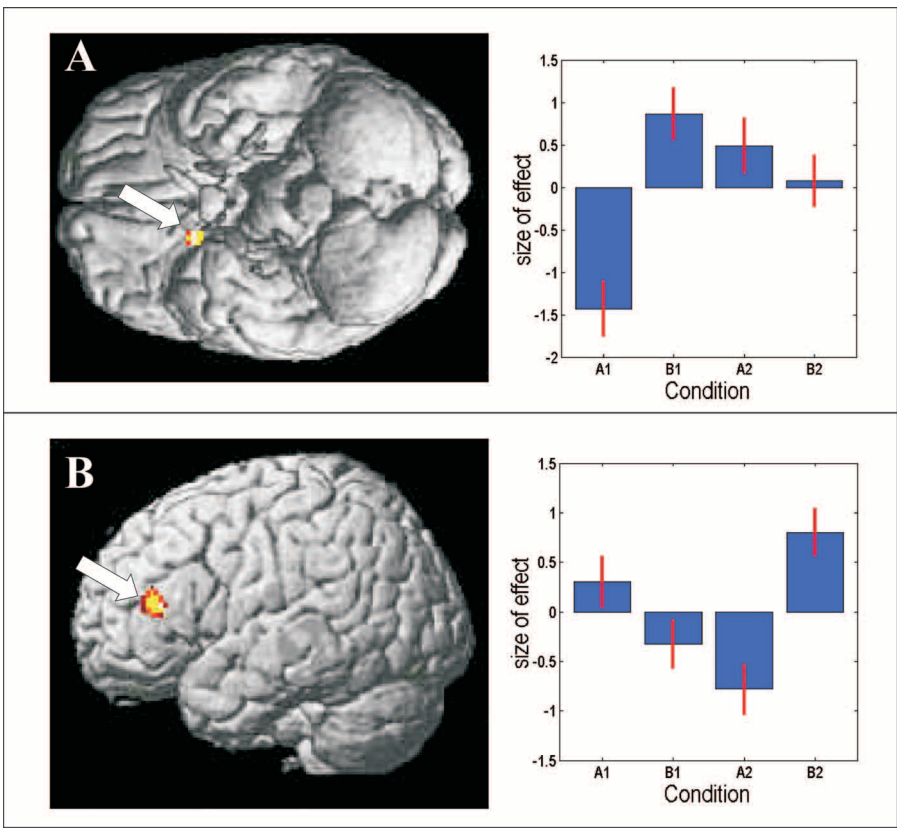

Figure 2. (A) Voxels in right posterior medial orbitofrontal cortex significant for the comparison subjectively experienced paralysis (active–rest) versus intentionally simulated paralysis (active–rest), represented on a rendered brain seen from the inferior aspect. Voxels are significant at $p < .001$ (uncorrected for multiple comparisons across whole brain). (B) Voxels in left ventrolateral prefrontal cortex significant for the comparison intentionally simulated paralysis (active–rest) versus subjectively experienced paralysis (active–rest), represented on a rendered brain seen from the left lateral aspect. After small volume correction (see results section) these voxels are significant at $p < .05$ (corrected for multiple comparisons). The corresponding plots of effect size are displayed adjacent to the rendered brain. VLPFC = ventrolateral prefrontal cortex; A1 = rest (subjectively experienced paralysis); B1 = active (subjectively experienced paralysis); A2 = rest (intentionally simulated paralysis), B2 = active (intentionally simulated paralysis).

previous study (Spence, Crimlisk, Cope, Ron, & Grasby, 2000), reported task-related hypoactivation in the left prefrontal cortex for patients with hysterical weakness compared to feigners (peak *Z*-score at coordinates $x = -48$, $y = 36$; $z = 28$), and on this basis we hypothesised that the comparison ([B2-A2]–[B1-A1]) would identify significant voxels in the left prefrontal cortex (either due to increased activation during intentionally simulated paralysis, or decreased activation during subjectively experienced paralysis, or both). A small volume correction was therefore performed employing a search volume of 20 mm radius centred at $x = -48$, $y = 36$, $z = 28$. With this small volume correction, the left ventrolateral prefrontal region was significant at $p < .05$ (corrected for multiple comparisons within the search volume of interest).

In the contrast ([B1-A1]–[B2-A2]), small volume corrections based on a priori hypotheses concerning relative overactivity during subjectively experienced paralysis (anterior cingulate cortex and orbitofrontal cortex; Halligan et al., 2000; Marshall et al., 1997) and relative hypoactivity during intentionally simulated paralysis (right anterior prefrontal regions; Spence et al., 2000), did not result in voxels significant at the threshold of $p < .05$, corrected for multiple comparisons. Although we report the activation of the right medial orbitofrontal cortex, our region is significantly posterior ($y = 12$ compared to $y = 54$) to that described by Halligan and colleagues in their single case (2000).

DISCUSSION

The study of patients with medically unexplained weakness has proved difficult (Ron, 2001). We therefore chose to examine in a group of normal subjects the distinction between a subjectively experienced limb paralysis and an intentionally simulated paralysis. By employing hypnosis as a cognitive tool we have been able to experimentally manipulate the subjective experience of paralysis within the same subjects, allowing us to examine for differences in patterns of brain activation between a subjectively experienced limb paralysis and an intentionally simulated limb paralysis. Our results support the notion that the neural mechanisms involved in the generation of these two behaviours are clearly distinct.

Before discussing our findings some general issues need to be raised. First, our subjects were all male whereas the majority of patients with conversion disorder are typically female. Our choice of male subjects was determined primarily by the radiation protection rules that apply to PET imaging in the UK. While this could limit the generalisation of our data with regard to laterality as well as to clinical populations, there is a clear precedent for the use of male subjects in these types of studies. The Spence et al. (2000) conversion disorder patients, for example, were also all males and, whereas the Marshall et al. (1997) conversion disorder patient was female, the single case study reported by Halligan et al. (2002), which used it as an experimental model, involved a male

participant. Similarly, we restricted our procedures to motor effects experienced in the left leg, which might again have implications for the interpretation of contralateral brain effects. We attempted to minimise effects on brain activations that might have been introduced by unintended changes in sensation in the two paralysis conditions by including in the limb paralysis script the suggestion that the paralysed limb would retain normal sensitivity. Participants' descriptions of their paralysis experience did not give any indication that they were experiencing their paralysed limb as heavy or numb, for instance.

Differential task related activations

The conjunction analysis demonstrated that during both subjectively experienced paralysis and intentionally simulated paralysis, requests to attempt to move the left leg compared to rest activated a number of regions demonstrated by previous neuroimaging studies, to be involved when preparing to move (Deiber, Ibanez, Sadato, & Hallett, 1996; Krams, Rushworth, Deiber, Frackowiak, & Passingham, 1998) and when imagining movement (Stephan et al., 1995). Thus the absence of leg movement in both paralysis conditions appears to be due to the failure of movement initiation, not of movement preparation.

A direct categorical comparison of task-related relative increases and decreases in activation in the two paralysis conditions, allows further exploration of the mechanisms involved in preventing or inhibiting movement initiation. Our most robust result is the relative increase in activation in the left VLPFC during intentionally simulated paralysis, consistent with the conscious volitional inhibition of the incipient motor response. The VLPFC is also thought to be involved in the learning of new associations between visual cues and motor responses (Passingham, Toni, & Rushworth, 2000), and it is possible that activation in the VLPFC seen in intentional simulators is due not only to the inhibition of a motor act, but the learning and maintenance of a new association between the auditory cue and the inhibition of movement. We identified the prefrontal cortex a priori as a region of interest, based on the only available comparison of a similar nature (Spence et al., 2000). A potential weakness of this approach is that the prefrontal region identified by Spence et al. as hypoactive for patients with hysterical weakness of the left arm compared to the feigners was labelled as DLPFC, whereas our activation is situated in the VLPFC. These authors described two peaks, one above, and one just below the inferior frontal sulcus, suggesting that their region involved both the DLPFC and VLPFC. Thus we feel that our results replicate in part that of these authors.

The remaining results failed to achieve significance once corrections for multiple comparisons across the whole brain are made. However, we include them in a descriptive capacity, in order that they may form the basis of future hypothesis-driven work in this field. The relative increases in task-related activity in the right intraparietal sulcus and superior temporal sulcus during

intentionally simulated paralysis may be related to continued preparation to move in this condition, as both have been associated with the preparatory set (Toni, Theonissen, & Zilles, 2001), and in addition, the superior temporal sulcus has been shown to be active during response inhibition (Toni et al., 2001). The relative overactivation of the medial parietal association cortex (precuneus) in the intentionally simulated paralysis condition is also interesting as this region has reciprocal connections with intraparietal sulcus and superior temporal sulcus (Leichnetz, 2001). This region is involved in higher order sensory integration and has been activated in states of self-awareness (Iversen & Mishkin, 1970). Intentionally simulating paralysis of the left leg in the face of continued instructions to move requires monitoring of both self and the changed significance of the cue (i.e., to do the opposite of the instruction and not move), thus it is not surprising that activation of a network of regions involved in higher order processing, integration, and monitoring is seen. We do not make the claim that this network is specific for deceit or feigning, but many of the cognitive processes required to perform such acts involve the network we have described.

An additional possibility is that the instructions given in the simulated paralysis condition are more complex that those in the subjectively experienced paralysis condition and that it is the increased load on verbal working memory which is responsible for the increased activity in the left prefrontal cortex rather than the experienced voluntariness of the task. That there is a difference in voluntariness between the two paralysis conditions depends on the subjective report of the participants. These reports could have been influenced by demand characteristics of the test situation when completing the retrospective VAS scales. This possibility was minimised by having the voluntariness questionnaires completed at a postscan debriefing session conducted by the informed experimenter in the absence of the observer/neurologist.

The absence of relative increases in prefrontal activation during subjectively experienced paralysis supports the assertion that the subjects cannot, rather than will not, move the leg. Instead, during this paralysis condition, we see relative increases in activation in the right orbitofrontal cortex as well as in the left putamen and thalamus, and right cerebellum (Figure 2A). Peak orbitofrontal activation in our group study is more posterior than in the single subject studied by Halligan et al., and is therefore described as a new region. Lesion studies in animals (Iversen & Mishkin, 1970) and humans (Fuster, 1989) have suggested that the orbitofrontal cortex is involved in behavioural and emotional inhibition rather than motor inhibition. Strong connections exist between the posteromedial orbitofrontal cortex and the adjacent ventral striatum, areas associated with the interaction between emotion, somatic representations of body state and volitional decision making (Bechara, Damasio, & Damasio, 2000), suggesting a possible mechanism of motor inhibition in our subjects with subjectively experienced paralysis.

We did not find relative overactivations in anterior cingulate cortex for the comparison ([B1-A1]–[B2-A2]), although in both of our previous case studies (Marshall et al., 1997; Halligan et al., 2000) the anterior cingulate cortex was found to be overactive during an attempted use of a subjectively paralysed limb compared to a control condition. This discrepancy is likely to be related to differences in experimental design. In the case studies, actual (restrained) movement was compared to preparation to move, whereas in the current study, attempted (unrestrained) movement was compared to rest. Not only were the active tasks different, but so too were the baseline tasks. To illustrate the point, in our study, direct comparison of attempting to move during subjective paralysis compared to attempting to move during feigning (B1–B2), did show significant relative overactivation in the anterior cingulate cortex. However, this comparison does not take account of baseline (i.e., it does not represent *relative* activation during attempted movement compared to rest in the two states), and has therefore not been formally reported. The role of the anterior cingulate cortex remains unclear.

Changes in rCBF related to hypnosis condition

The experimental question required that we include hypnosis as a condition throughout all scans if inferences about the underlying intentional set were not to be confounded with the presence or absence of hypnosis. Accordingly, we are unable to say anything about the cerebral effects of hypnosis *per se*. That said, there were differences between the rest states in the two paralysis conditions. Indeed, we anticipated this possibility, and so each active task was matched with a separate rest task performed in the context of the same paralysis condition. Therefore, our results pertain to the relative changes in rCBF between an active task and its matched rest condition. The differences between the two baseline conditions do not affect inferences about task-related activations, which is the subject of this paper. One possible reason for a difference in the rest conditions is that suggestions for limb paralysis might have served to intensify the hypnosis in the subjectively experienced paralysis condition, whereas the instructions to deliberately feign a paralysis could have had the reverse effect. There was, however, no evidence for systematic difference in hypnotic depth between the two paralysis conditions either from the subjects' retrospective reports, postscan finger signalling or from general observation by the experimenters.

CONCLUSIONS

We used hypnosis to create two behaviourally indistinguishable versions of the same motor behaviour (or neurological symptom) in the same subjects, differentiated only by their subjective characteristics and the intention to deceive an observer for material gain. On the strength of these results, we suggest that the cognitive processes involved in preventing movement during subjectively experienced paralysis involve different cerebral networks compared to those

engaged when subjects intentionally simulate the same paralysis. The results of our study are directly relevant to subjectively experienced motor paralysis produced by suggestion following hypnotic induction, and may not readily transfer to patients with conversion disorders. Conversion disorders are arguably more complex, and the underlying mechanisms are likely to change with circumstance and in particular chronicity. Equally, although we have attempted to create experimentally the necessary conditions of insight, intentionality, and motivation, there may be differences between our intentional simulation condition and true malingering. Nevertheless, using hypnosis we have been able to manipulate relevant experimental variables in order to study central aspects of the practically and theoretically crucial distinction between conversion disorder and malingering in normal controls. In addition a possible link between conversion paralysis and hypnotically induced paralysis is suggested by the available neuroimaging evidence (Halligan et al., 2000; Marshall et al., 1997), and this may be a fruitful avenue to pursue further. In particular, hypnosis may provide a useful means with which to isolate key elements thought to be involved in symptom generation, and to study them in a controlled fashion. Most importantly, the present study provides the basis for extending formal research on the controversial issue of the relationship between will, intention, and action (Haggard, Clark, & Kalogeras, 2002).

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