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The alien hand syndrome: What makes the alien hand alien?

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The alien hand syndrome is a deeply puzzling phenomenon in which brain-damaged patients experience their limb performing seemingly purposeful acts without their intention. Furthermore, the limb may interfere with the actions of their normal limb. We report a case of alien hand syndrome following a left medial frontal and corpus callosum ischemic lesion. From our clinical observations and the patient's performances on experimental tasks, we postulate that three factors contribute to the sense of alienness: First, the errant limb must be disinhibited and disproportionately reactive to external environmental stimuli. Second, the limb is under less volitional control and produces perseverative movements in which motor stereotypies are concatenated. Consequently, the disinhibited limb perseverates on external stimuli and appears purposeful, despite not being engaged in true goal-directed intentions. Finally, the patient needs to have a relatively intact action-monitoring system to be aware of the abnormal movements as they are occurring.

INTRODUCTION

The alien hand syndrome (AHS) is one of the most dramatic and puzzling syndromes encountered in clinical neurology. Patients with this syndrome experience their limbs acting without being guided by their own will (Biran & Chatterjee, 2004; Bogen, 1993; Brion & Jedynak, 1972; Cooney & Gazzaniga, 2003; Feinberg, 1997; Fisher, 2000; Gasquoine, 1993; Kertesz, 2000; Marchetti & Della Sala, 1998; Trojano, Crisci, Lanzillo, Elefante, & Caruso, 1993) They are unable to stop their alien limb from reaching out and seizing objects, and they often have to use their other hand to prise open their fingers to release the object (Kumral, 2001; Ong Hai & Odderson, 2000). Patients with AHS have even woken up to find their alien limbs choking them

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(Banks et al., 1989). Perhaps the most peculiar abnormal movement in the AHS is diagonistic apraxia (Akelaitis, 1944–1945; McNabb, Carroll, & Mastaglia, 1988; Nishikawa et al., 2001; Tanaka, Iwasa, & Yoshida, 1990; Tanaka, Yoshida, Kawahata, Hashimoto, & Obayashi, 1996), in which one hand acts in opposition to the other. For example, a patient reported by Bogen (1993) found his alien hand undoing the buttons of his shirt even as his "healthy" limb tried to button the shirt. Patients frequently express astonishment and frustration at these errant limbs and often refer to the limb in the third person.

The syndrome, in its typical and dramatic form, arises most commonly following lesions to the medial frontal lobes and the corpus callosum (Banks et al., 1989; Baynes, Tramo, Reeves, & Gazzaniga, 1997; Bogen, 1993; Chan & Liu, 1999; Della Sala, Marchetti, & Spinnler, 1991; Fisher, 2000; Goldberg & Bloom, 1990; Goldberg, Mayer, & Toglia, 1981; Suwanwela & Leelacheavasit, 2002). A variant of the syndrome can be seen with thalamic or parietal damage (Bundick & Spinella, 2000; Levine & Rinn, 1986; Marey-Lopez, Rubio-Nazabal, Alonso-Magdalena, & Lopez-Facal, 2002; Nishikawa et al., 2001; Ventura, Goldman, & Hildebrand, 1995) and with cortico-basal degeneration (Kompoliti et al., 1998).

The syndrome itself is quite variable; indeed it may be sufficiently variable that it encompasses different syndromes. For example, patients vary in the extent to which they claim ownership of their limb and recognize their own limb and in how they describe their errant limbs. (For an extended discussion of the terminological ambiguities accompanying this variability, see Della Sala et al., 1991; Marchetti & Della Sala, 1998.) One might further infer that different expressions of this syndrome are associated with different pathology. For example, medial prefrontal damage, especially on the left, is hypothesized to be associated with grasping behaviours and compulsive utilization behaviours (Boccardi, Della Sala, Motto, & Spinnler, 2002; Eslinger 2002), callosal damage with intermanual conflict (Feinberg, Schindler, Flanagan, & Haber, 1992), and posterior lesions with disorders of motor control because of interrupted sensory feedback (Marey-Lopez et al., 2002). However, these brain–behaviour relationships are not always consistent (as reviewed recently: Scepkowski & Cronin-Golomb, 2003) and the claims are largely based on descriptive data. Patients with this syndrome have only rarely been investigated experimentally (Giovannetti, Buxbaum, Biran, & Chatterjee, 2005; Riddoch, Edwards, Humphreys, West, & Heafield, 1998; Riddoch, Humphreys, & Edwards, 2001) in attempts to test hypotheses of component processes that might give rise to features of the syndrome. Riddoch and colleagues (1998, 2001) found that a patient with cortico-basal degeneration and AHS had difficulty inhibiting prepotent responses with familiar objects in familiar positions. They emphasize the conflict between goal-based intentional movements and stimulus-driven unintentional movements as an important element in the errors made by this patient.

In the case presented here, our goal is to frame the investigations within classic views of motor control (Chatterjee, 1998; Denny-Brown, 1958; Jackson, 1958; see also related models by Norman & Shallice, 1986) and relate them to more recent ideas of action monitoring and forward models of motor behaviour (Desmurget & Grafton, 2000; Wolpert, Ghahramani, & Flanagan, 2001). We recognize that variants of the syndrome may have different underlying mechanisms and hope that this general approach might be useful in identifying such mechanisms in the forms of AHS in which abnormal motor output is evident. The investigations are motivated by three ideas: motor systems are organized hierarchically, the nervous system controls both approach and avoidance motor behaviours, and approach motor behaviours lie on a continuum of being externally evoked (exo-evoked) or internally driven (endo-evoked).

First, the motor system has a hierarchical organization with different levels of complexity as articulated in the nineteenth century by Hughlings Jackson (Jackson, 1958). Simple movements such as grasping, pinching, or pointing serve as motor primitives. These motor primitives may be concatenated into more composite actions that may still remain stereotypic but ultimately serve complex goal-directed behaviour. The neural representation of motor primitives is not well understood (Ghahramani, 2000) but may originate in the parietal lobes (Colby, 1998; Denny-Brown, 1958; Milner & Goodale, 1995). The frontal cortex coordinates motor primitives generated by the parietal lobes into integrated goal-directed behaviours. Following frontal damage, motor primitives are often released as perseverative movements. As described originally by Liepmann (described by Sandson & Albert, 1984), perseverations can also vary in their level of complexity. The question with respect to AHS is, at what level within this hierarchical organization is the abnormal limb operating?

Second, Denny Brown thought that goal-directed behaviours relied on parietal and frontal interactions, with the parietal cortex controlling approach behaviours and the frontal cortex controlling avoidance behaviours (Denny-Brown, 1958). On this view, frontal damage releases parietal approach behaviour that can take the form of simple reflexive acts such as grasp behaviours or more complex actions such as the compulsive and automatic manipulation of tools seen in utilization behaviours. The question with respect to AHS is, what is the nature of the approach behaviours in this disorder?

The third idea motivating our experiments is the distinction between exo-evoked and endo-evoked movements, as also emphasized by Riddoch and colleagues (1998, 2001). Exo-evoked movements are relatively autonomous movements that are triggered and shaped by objects in the environment. Endo-evoked movements are volitionally planned movements with complex goals in mind. Many situations rely on combinations of both endo- and exo-evoked movements. Thus, when writing a letter, one may reach and grasp a pen on the table relatively autonomously but consciously plan the motor programs involved in actually writing the letter. The question with respect to AHS is, how has the relationship between endo- and exo-evoked movements changed for the abnormal limb?

With this framework as a guide, we report our clinical and experimental observations of a patient with AHS. We designed the experiments to address different kinds of movement, from simple responses to more complex goal-directed actions. We recently reported this patient's behaviour in the complex naturalistic action of making coffee (Giovannetti et al., 2005). Those data are also summarized here (in Experiment 4), but the focus here is on control over less complex movements. At the outset, it should be clear that the AHS is a rare syndrome with sparse experimental literature to guide these investigations. Our experiments are by definition exploratory. Our interpretation of the experimental results is shaped by clinical observations as well as comparisons to the phenomenology of other dramatic motor syndromes, such as hemiballismus and utilization behaviour. From our observations and data, viewed through classic and contemporary models of motor control, we hope to gain some insight into the most interesting and also the most elusive aspect of the AHS: patients' subjective sense of their own limbs' alienness.

CASE REPORT

JC was a 56-year-old right-handed man who suffered a left hemispheric stroke and presented initially with mild right-sided weakness and naming difficulties. His MRI scan demonstrated a left fronto-mesial lesion extending into the rostrum, body, and splenium of the corpus callosum (see Figure 1). Initially he did not use his right arm spontaneously, and it remained largely inert. Four weeks after the stroke he complained of peculiar uncontrolled movements of this limb. His hand would do things "as though it has a mind of its own"—such as playing with light switches, grasping and holding things. It opposed the left hand in some situations. For example, it would grab the left hand or reach for papers held by the left hand. Eating became difficult because of oppositional behaviour of the right

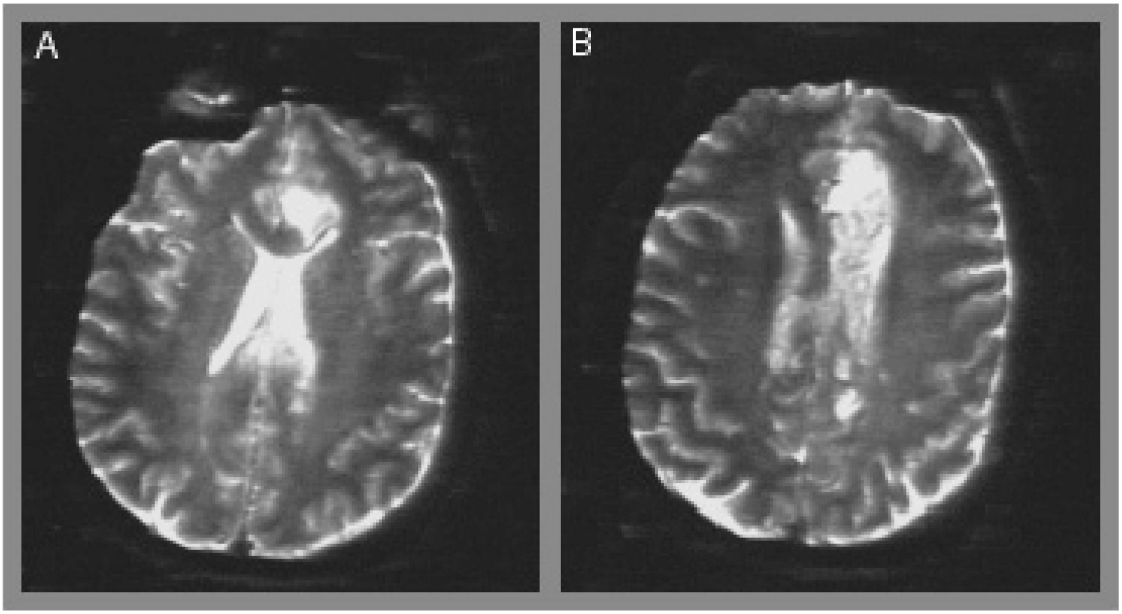

Figure 1. *Axial T2 MRI scan demonstrating the left mesial frontal lesion (A) and the extension to the corpus callosum (B).*

limb. At night after he would fall asleep, the limb continued to move and would frequently wake him up by seizing parts of his body. JC moved his bed against a wall so that he could lie with his right arm trapped between his body and the wall in the hope that he would rest through the night. During the day, he frequently sat on his right hand to keep it from moving or grasped a rolled up magazine in this hand, which he said, "satisfied" the hand.

On the general neurological examination 2 months after the stroke JC's cranial nerves were intact. He did not have any motor weakness. All reflexes were symmetric, and there were no pyramidal signs. He had a grasp reflex with his right hand. There was no sensory loss. His coordination and gait were normal.

On his bedside mental examination, JC was fully alert and oriented. He had a digit span of 6 digits forward and 4 digits backwards. His short- and long-term memory were intact. His speech was well articulated. His comprehension and naming were normal. He was apraxic when miming how to use tools with his left hand (Kischka, Ettlin, Lichtenstern, & Riedo, 1996). He did not show other signs of callosal impairment. He could name objects held in his left hand (without visual feedback), and he could identify letters and numbers traced on his left palm. He was perseverative when drawing triple loops and was unable to write alternating *m*s and *n*s in script. He had difficulty coordinating sequential gestures and their names (fist, edge, palm) with either hand. He was also unable to coordinate his two hands in an alternating simple motor sequence, such as alternating clenching one hand and extending the other in a rhythmic pattern. He could coordinate alternating sequences cognitively, as demonstrated by his ability to perform an oral version of Trail-Making B (Report A-1, B-2, C-3, and so forth).[1]

[1] We administered a non-standardized test, as sometimes used by neurologists at the bedside as a coarse measure of frontal lobe function.

Further limb signs and symptoms

The following descriptions of JC's right-hand abnormalities are based on behavioural observations during his visits and a diary kept by the patient and his wife. These abnormal behaviours occurred during the day and night and were observed across many activities, including eating, reading, self-grooming, and sleeping. The abnormal behaviours were combinations of unresponsiveness (negative phenomena/akinesia) and uncontrolled movements (positive acts).

Unresponsiveness

At times the right hand would not carry out JC's intentions. This unresponsiveness was often combined with positive uncontrolled behaviour. For example, while he was cleaning his house, the alien hand might dust only part of the furniture. When he was showering, it might avoid holding the soap. When eating, it might not reach for a cup of tea or pick up food with a fork even though it was grasping the fork.

Uncontrolled actions

These actions were either related or unrelated to JC's intentions. They are characterized as follows:

Simple repetitive movements. JC frequently repeated simple intransitive movements. For example, he would move his right hand side-to-side, tap his knee, or scratch his shoulder repetitively without intending to do so. Similar perseverative movements were also seen with transitive movements. For example, he would repeatedly turn the water tap on and off, put eyeglasses on and off, or repeatedly press keys of remote controls.

Complex continuous actions. These movements were often intentionally initiated by JC, but he was unable to stop the right arm once the movement was initiated. These repetitions could occur when he brushed his teeth, swept the floor, combed his hair, or cleaned his eyeglasses. On one occasion the right hand kept pouring tea from a kettle with boiling water even after the cup was filled. When getting on a bus, the right hand might take a card out of his pocket but not his tokens, while in other instances it reached for tokens in his pocket for no apparent reason. Occasionally, these seemingly complex continuous behaviours were observed without JC's knowledge. For example, in one of the testing sessions, he was asked to turn pages of a magazine with his left hand. As he did this (without any difficulty), the examiner lightly touched his right fingers with a pen. The right hand reached towards and persisted in following the pen continuously as it was slowly moved away from the hand (see Figure 2). This reaching continued until the limb was a foot above the table. JC was unaware of his arm moving on that side.

Intermanual conflict. In some situations the right hand acted at cross-purposes to the left hand. Sometimes it would interfere with the left hand while it was performing actions. Examples of such behaviours included snatching a knife out of the left hand while JC tried to cut food, or seizing papers held in the left hand, interfering with the left hand while shuffling cards, refusing to let the left hand put on a belt. At other times it would undo actions immediately after they were completed by the left hand. For example, it would take the shirt-tails out of JC's trousers after he had tucked the shirt in with his left hand. The patient's wife also observed the hands "fighting" while JC slept.

Subjective reactions to the hand

JC attributed wishes and plans to his right limb. These attributions were evident in statements such as "It has a mind of its own", "Wants to be the boss", "Its own way", "Wants to dust the way it wants", "It won't go the way I want", "Controls the towel while I dry myself". JC further interpreted simple reaching movement of his right hand as purposeful: for example, "[The] right hand goes in [my] pocket to check for them [tokens]". He reacted to the actions of the right hand quite vividly at times by cursing it ("Damn you"), or by restraining it (sitting on it, seizing it with his left hand, holding it between

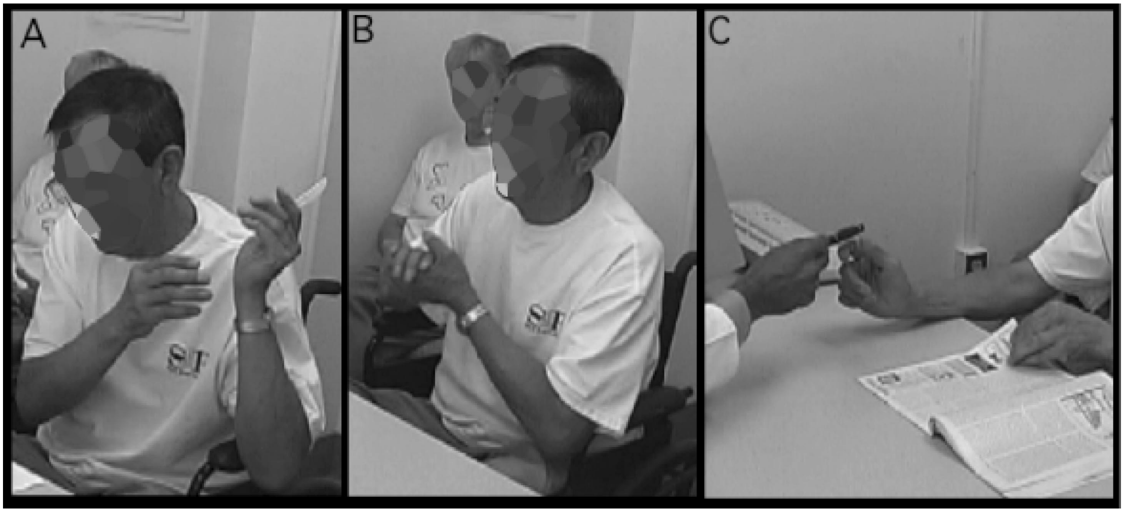

Figure 2. *Examples of alien behaviour of the right hand: (A) The right hand grabbing knife from the left hand. (B) The left hand is restraining the right hand. (C) JC reading a paper, unaware of his right hand reaching for a pencil.*

his legs—see Figure 2). His wife described the right hand as acting like a "toddler in a bad mood".

EXPERIMENT 1: SIMPLE SELECTIVE ACTION

Our clinical observations suggested that JC's right limb was disinhibited. To test the hypothesis that JC's limbs reacted differently, and the right was relatively disinhibited and responded reflexively to exogenous stimuli, we designed a selective reaction task in which he responded with either his right or his left hand on every trial in response to a cue on a computer monitor. In different blocks the ratio for the response of each hand was varied to determine the extent to which response biases for both hands would be influenced by contextual factors, specifically the probability of making a response. Our prediction was that JC's right hand would be disinhibited, and we wished to learn whether it would be more sensitive to contextual contingencies than the left hand.

Stimuli consisted of the letters "R" or "L" presented for 150 msec at the fixation point. At a viewing distance of 60 cm, each letter subtended a vertical and horizontal visual angle of approximately 1.5° and 0.5°, respectively. JC's index fingers were located on the target keys (right index finger on the "L" key and left index finger on the "F" key. The letters were masked by white stickers. JC was asked to respond with the hand designated by the letters stimuli ("R" for the right hand, and "L" for the left hand). There were 3 conditions differing in the ratio of the stimuli given to each hand (L4:R1, L1:R1, L1:R4). Accordingly, there were 3 kinds of trials:

1. Frequent trials (F), in which the designated hand in a trial was frequently the stimulus for the condition (i.e., "L" stimuli in the L4:R1 condition, or "R" stimuli in the L1:R4 condition).
2. Infrequent trials (I), in which the designated hand was as the infrequently the stimulus of the condition (i.e., "L" stimuli in the L1:R4 condition, or "R" stimuli in the L4:R1 condition).
3. Equal-frequency trials (E), in which both stimuli appeared with equal frequency (i.e. "R" or "L" stimuli in the L1:R1 condition). There were 240 trials for each condition, given in four 60-trial blocks.

Results

Accuracy

JC made more errors of commission (inappropriate responses) with his right than his left hand. This difference was significant for all trial types testing for the significance of proportional differences (Bruning & Kintz, 1977): 31% versus 13% for the equal-frequency trials ($p < .0001$), 33% versus 15% for the frequent trials ($p < .012$) and 8% versus 1% for the infrequent trials ($p < .0001$).

Reaction times

The reaction times (RT) are shown in Figure 3. RTs for correct trials were analysed further. RTs greater than 2 standard deviations from the mean for each condition were considered outliers and were not included in the analyses. ANOVA revealed a main effect for frequency (RTs were faster with more frequent trials: $F = 17.19$, $p < .0001$) and hand (right hand was faster than left: $F = 23.58$, $p < .0001$). There was a Frequency × Hand interaction, such that the trial frequency influenced the right more than the left hand ($F = 6.48$, $p < .005$).

Post Hoc comparisons demonstrated that the right hand was faster than the left hand in the frequent and equal-frequency conditions and that while the RTs of the right hand in the frequent

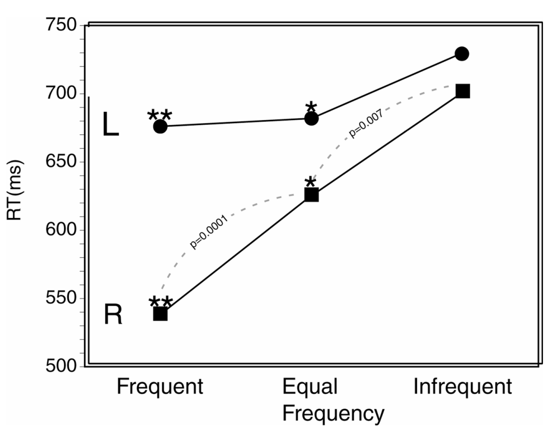

Figure 3. *RTs for the various conditions in the choice reaction task (*p = .01, **p < .005).*

and infrequent conditions differed significantly from the equal-frequency condition (F vs. E: $F = 21.0$, $p < .0001$; I vs. E: $F = 7.3$, $p < .01$), those of the left hand did not. This analysis suggests that the Hand × Frequency interaction originated in the right hand's greater sensitivity to contextual probabilities.

Comment

These data is consistent with the view that JC's right hand was disinhibited as compared to his left. When compared to the left, it responded faster and more often inappropriately, and it was influenced to a greater degree by contextual probabilities. This reactivity to environmental and contextual cues with disinhibited reflexive movements may have contributed to JC's sense of the limb's alienness.

EXPERIMENT 2: SELECTION AND SEQUENCING COMPLEX ACTIONS

JC claimed that at times his limb would not respond to his intentions in everyday tasks, such as dusting. To test the hypothesis that JC had less control over volitional sequencing of his right than his left hand, we designed a task with two components. The first component was similar to the previous experiment and assessed his reactivity to selecting the use of his left or right hand. The second component involved sequential movements to different keys indicated by a sequence of colours shown on the screen. On each trial these stimuli would indicate one of three possible combinations of movements.

We were specifically interested in the difference between the two hands, rather than in whether one or the other was "normal". On clinical examination it was JC's left arm that demonstrated a callosal apraxia and would be likely to have trouble with sequences of previously learned motor acts. If anything, this observation might predict worse performance on sequencing by the left than the right hand. By contrast, if the right hand was under less volitional control in on-line planning of novel sequences, then it would perform less well than the left when manoeuvring through these sequences that varied across trials.

Stimuli consisted of the letters "R" or "L" presented at a fixation point (viewing distance of 60 cm, each letter subtending a vertical and horizontal visual angle of approximately 1.5° and 0.5°, respectively) and a vertical array of 3 coloured oval shapes (red, green, and yellow) presented below the fixation point and subtending a vertical and horizontal visual angle of 1.5° and 5°, respectively. Letter and colours were presented simultaneously. The stimuli remained on the screen until the end of each trial. See Figure 4 for illustration of the experiment. All combinations of letters and colours were counterbalanced. JC responded with 4 movements: 1st, 2nd, and 3rd step: pressing coloured keys ("K": yellow, "H": red, "F": green), 4th step: pressing the space bar. At the onset of each trial JC's hands were placed in front of the keyboard rather than at the keys themselves, as in the previous experiment. Accordingly, on the first step of each trial he reached towards the keyboard with the appropriate hand, while in the following trials his hand was in the vicinity of the target keys. The examiner recorded the hand that responded (right, left, or both hands). The computer recorded the time taken to make each movement. There were 2 blocks of 30 trials each.

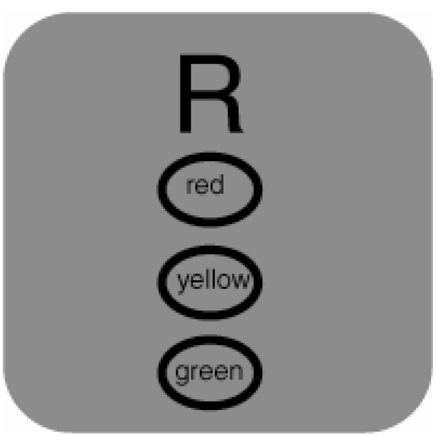

Figure 4. *In this trial JC was required to press with the right hand the following key sequence: "H" (Red) → "K" (Yellow) → "F" (Green) → space bar. The colour names denote the actual colour of the ovals. In the experiment the words were not present.*

Results

Accuracy

JC was similarly accurate for all movements with either hand (R = 27/30, L = 28/30, $p = ns$). His rare errors were the following: For the right-hand trials he produced the wrong sequence twice and used the wrong hand once. For the left-hand trials he produced the wrong sequence once and used the wrong hand once.

Reaction times

The right hand was faster than the left on the first movement (right hand: 2069 ms, left hand: 2685 ms, $p < .02$). By contrast, the right hand was slower than the left for the subsequent movements (right-hand average: 621 ms, left-hand average: 517 ms, $p < .005$. (See Table 1 and Figure 5.)

Comment

This task demonstrated a difference in the performances of both hands with respect to the two components of the task. The right hand was faster than the left when responding reflexively, replicating the results of the previous experiment. However, it was slower than the left when manoeuvring through a complex novel motor sequence that had to be planned on every trial. These results are compatible with our hypothesis

Table 1. *Performance of hands in the different steps of the multi-step task*

Step	*Hand*	*RT*[a]	*SD*
1*	Left	2685	1207
	Right	2069	406
2–4**	Left	517	167
	Right	621	274

[a]In ms.
*$p = .0165$. **$p = .0035$

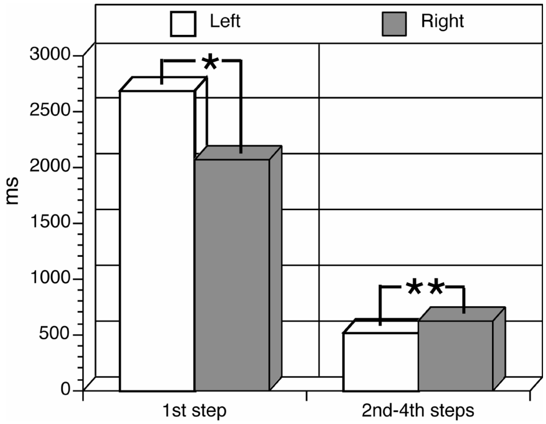

Figure 5. *Performance of hands in the different steps of the multi-step task (*$p < .02$, **$p < .005$).*

that the subjective sense of alienness might emanate from having a limb that is simultaneously disinhibited and under less volitional control in planning sequences of movements.

EXPERIMENT 3A: ACTION MONITORING, MOTOR TASK

In this experiment we examined JC's reaction to his own errors. To do so, we relied on an observation made initially by Rabbit (1966). The observation is that when subjects engage in a task with serial responses, a correct response that immediately follows an error is slower than other correct responses. The idea is that when an action-monitoring system is more careful after it detects an error, it is consequently slower on the subsequent trial. The normal monitoring of such errors is thought to be modulated by the anterior cingulate gyrus (ACG) and the dorsolateral prefrontal cortex (Gehring & Knight, 2000). Damage to this system could impair JC's awareness of his aberrant motor behaviour in two hypothetical ways. First, a disinhibited errant limb might simply be the result of poor monitoring of this limb. Alternatively, intact action monitoring of errors could contribute to the sense of alienness if JC detected the disinhibited nature of his right-limb movements even as it moved.

We modified a task used previously by Gehring and Knight (2000). The goal was to design a task that would produce enough errors that the performances in error trials and in trials following errors could be evaluated. Rather than looking at group effects, as is more often done, we sought to find effects within an individual. Furthermore, rather than have subjects respond with both hands, JC responded with the same hand in each block. This modification was necessary because the hypothesis under consideration is not that JC had abnormal error monitoring, but that his monitoring ability was different for both hands. We also asked JC to rate his performance subjectively.

JC and 3 normal controls matched for age (average age = 54.3 years) performed a letter-discrimination task in which, following a cue, they chose one of 2 letters. The cue was a colour (specified by a word), and the subject had to choose the letter coloured by the cued colour. In each trial the cue (the word "green" or "red") was presented for 200 ms and was followed 400 ms later by a pair of letters (MM, MB, BM, BB), one of which was red and the other green. At a viewing distance of 60 cm, letters subtended a vertical and horizontal visual angle of approximately 1.5° and 0.5°, respectively. The subject had to press the key corresponding to the letter coloured in the cued colour. For the right-hand trials his index finger were placed on the "b" key and his middle finger on the "m" key; placement was the opposite for left-hand trials. The letters remained on display until the trial was completed. The inter-stimulus interval was 100 ms. See Figure 6 for the layout of the experiment. There were 960 trials for each hand, administered in 15 blocks of 64 trials each. After each block, subjects were asked to rank the performance of the hand on a scale of 1 (worst) to 5 (best).

Results

Accuracy

Results are shown in Table 2. Control subjects were more accurate than JC (left hand: 96.4% vs. 66.3%, $p < .0001$; right hand: 96.8% vs. 81.2%,

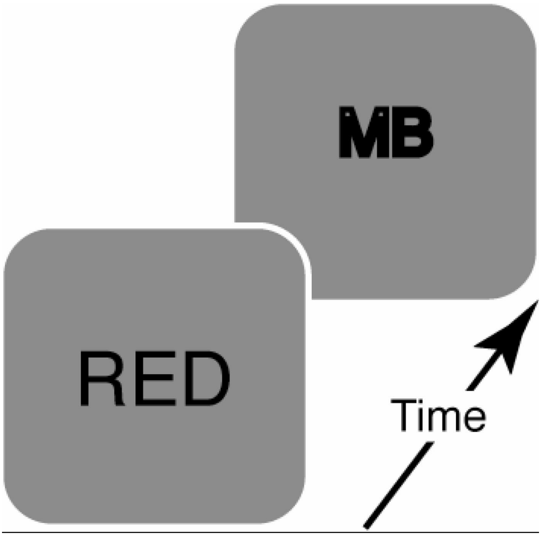

Figure 6. *Layout of the error-monitoring experiment. In this trial, following the cue, "RED" subjects were presented with the letter "M", which was coloured green, and the letter "B", which was coloured red; they had to respond by pressing "B".*

$p < .0001$). JC was more accurate with his right than his left hand ($p < .0001$).

Subjective rating
Control subjects rated the performance of their right hand as better than the left hand (LH = 3.6, RH = 3.9, $p < .05$). By contrast, JC rated the hands equally (LH = 2.3, RH = 2.2, p = *ns*), even though he was less accurate with his left hand.

Reaction times
Results are shown in Table 2 and Figure 7. Control subjects were faster than JC for both hands. They also had similar RTs for both hands. JC's pattern of performance varied with the two hands, as described below.

Different trial conditions. Control subjects were slower in both error trials and correct-posterror trials compared with the average correct trials (see Figure 5, $p < .0001$, for all comparisons to average correct). JC was slower on error than correct trials for the right hand ($p < .0001$) but not for the left hand (p = *ns*). He did not show slowing in the posterror trials. However, in correct trials preceding error trials the right hand was faster than its average correct performance ($p < .005$). This pre-error quickening was not observed with JC's left hand, or with either hand in the normal subjects.

Comment

On this task control subjects demonstrated a similar pattern of behaviour for both hands,

Table 2. *Performance in correct and error trials for JC and controls*

		JC				*Controls*			
	Hand	*RT*	*SD*	*N*	*p*[a]	*RT*	*SD*	*N*	*p*[a]
Correct: average	Left	1462	644	637	—	931	458	2777	—
	Right	1359	1690	780	—	887	400	2788	—
	P (r−l)				0.0082				0.0003
Correct: pre-error	Left	1425	601	209	0.482	866	332	91	0.18
	Right	1224	599	138	0.0030	861	316	78	0.62
	r−l				0. 0067				0.67
Error	Left	1433	705	323	0.55	1185	590	103	0.0001
	Right	1690	1108	180	0.0001	1158	733	92	0.0001
	r−l				0.0002				0.40
Correct: posterror	Left	1422	638	206	0.45	1365	883	89	0.0001
	Right	1278	628	134	0.19	1306	819	76	0.0001
	r−l				0.0514				0.94

[a]*p* values compared to correct average.

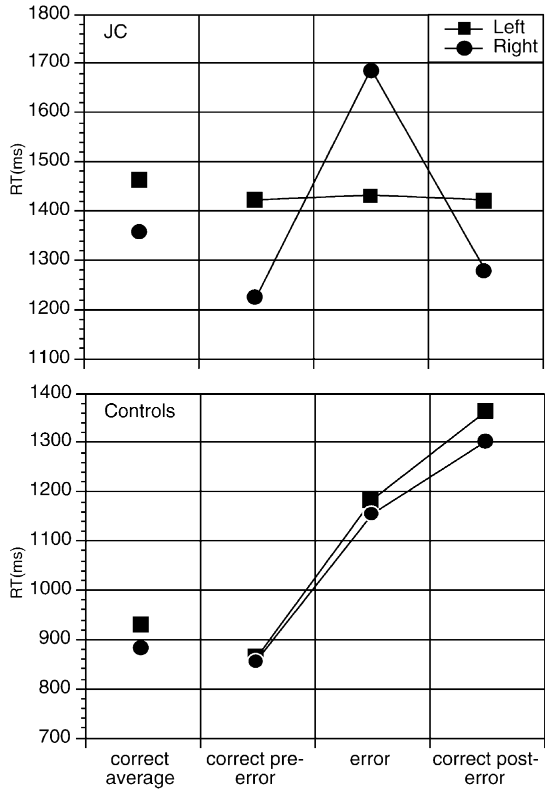

Figure 7. *Performance of the right and left hand in error and correct trials for JC (top) and control subjects (bottom).*

consisting of slowing on error and posterror trials. The slowing on posterror trials is compatible with the expectation that an error-monitoring system becomes more conservative after detecting an erroneous response. However, the slower responses on error trials themselves are at odds with the usual speed–accuracy trade-off in which error trials are expected to be faster than the average correct responses (Fitts, 1954). We are left to conclude that this error-slowing behaviour is idiosyncratic to this version of the task (in which all responses are made uni-manually). On this task, subjects become aware of their error even as they are making their erroneous movement.

Unlike the control subjects, JC performed differently with each hand. His left hand had similar reactions on error trials and on the correct responses that preceded and succeeded the error trial. By contrast, the right hand was variable, depending on the nature of the trial. It was slower on error trials and actually faster on the trial preceding the error trials in comparison to average correct trials. The slower responses on error trials by JC's right hand, similar to normal subjects, suggest that he was more aware of the error being made by his right hand. We do not know why JC did not show slowing on the trial following the error with the right hand. One possibility is that the effects of disinhibition may have countered the effects of posterror slowing on this trial for JC in a way that did not apply to normal subjects.

An unanticipated finding was that JC was faster on the trial before the error trial. This pre-error quickening suggests that his hand was speeding up in the preceding trial, and perhaps this acceleration predisposes him to making errors. This notion would be analogous to the clinical phenomenon of "festination" seen in patients with frontal-basal ganglia disorders, where they repeat a motor behaviour (often in walking) with increasing rapidity, until they lose control.

Control subjects rated the right hand as performing better than the left hand, compatible with their faster performance with the right than the left hand. JC, however, rated the performance of both hands similarly, although he was in fact faster and more accurate with the right hand. From this discrepancy, we again infer that he is more aware of the errors of his right than his left hand. This relative lack of awareness of his left hand is compatible with the observation that this hand's speed is not modulated by error or peri-error trials.

EXPERIMENT 3B: ACTION MONITORING, STROOP INTERFERENCE

In the previous experiment, our inferences about JC's monitoring of his limb movements were based on the different performances by each of his hands. Here, we wished to examine the integrity of his monitoring system more generally.

Medial frontal damage may produce dissociations between the selection of verbal and motor responses (Turken & Swick, 1999). Similarly, there might be a dissociation of monitoring abilities depending on whether the subject produces a motor or a verbal response. We examined JC's performance on a more commonly tested interference task, the Stroop task. We wished to learn if he could generate monitoring effects seen in normal subjects, despite his medial frontal lesion, which included the anterior cingulate cortex. JC's individual data were culled from a separate group study examining cognitive control in patients with ventral-medial prefrontal damage (Fellows & Farah, 2005).

This computerized version of the Stroop task required subjects to name one of 5 colours of ink in which single words were printed, as quickly as possible, as they were shown on the screen, one at a time. All words were the names of the same 5 colours—hence, all trials were either congruent (ink colour and word the same) or incongruent (ink colour and word different). Stimuli were on screen until the subject answered, with an intertrial interval of 1000 ms. The onset of the verbal response was recorded by a microphone connected to a PsyScope button box (Cohen, MacWhinney, Flatt, & Provost, 1993). Subjects had 70 practice trials, with equal numbers of congruent and incongruent stimuli. This was followed by 2 blocks of 100 trials each, separated by a rest period. The first, low-conflict, block had 80 incongruent trials and 20 congruent trials; in the second, high-conflict, block, this ratio was reversed. JC's data are compared to 12 age-matched normal control subjects.

Results

Similar to normal subjects, JC showed a normal Stroop interference effect that was modulated by the probability of being presented with conflicting stimuli. (Stroop effect: high-conflict condition, JC: 147 ms, controls: 171 ms; low-conflict condition, JC: 132 ms, controls: 106 ms). In addition, JC showed posterror slowing that was at least as robust as that of normal subjects. His responses on the posterror trials were 19% slower than on correct trials, whereas for normal subjects it was 6% (+11%) (Figure 8).

Comment

From these data, we infer that JC is capable of monitoring his actions in a cognitive interference task. Despite his medial frontal damage, he generates a pattern of interference and posterror slowing that is similar to normal subjects. Thus, the differences in the previous experiment between his action monitoring of the left and right hand are unlikely to be accounted for by a general abnormality of action monitoring. We conclude, albeit tentatively, that his monitoring of actions is different for each hand, and that he is disproportionately sensitive to errors made by his alien hand.

EXPERIMENT 4: NATURALISTIC ACTIONS—THE COFFEE CHALLENGE

Thus far, JC's motor behaviour was studied in constrained laboratory tasks. However, the phenomenology of AHS is most evident in everyday

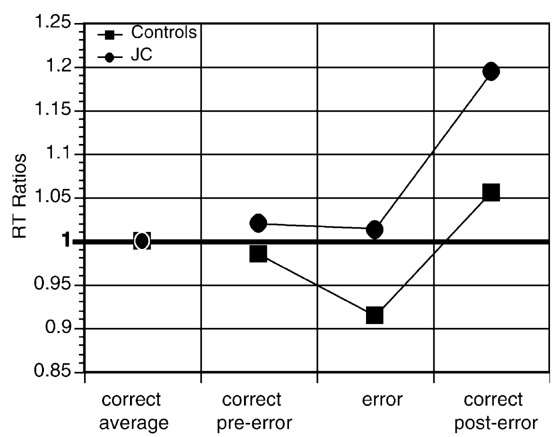

Figure 8. *Performance in the Stroop task in error and correct trials for JC and controls. The Y-axis denotes the ratio between the average reaction time in each condition and the average reaction time for correct trials.*

naturalistic tasks. To determine whether similar patterns of behaviour could be observed in actions that more closely simulate real-world behaviour, we used the coffee challenge (CC) task, in which subjects are required to prepare 2 cups of coffee. This is a task that has been given to a group of 17 healthy control participants (see Giovannetti, Libon, & Hart, 2002, for details on the design of the task, scoring procedures, and reliability). A comprehensive report on JC's bimanual performance on this task is described elsewhere (Giovannetti et al., 2005). In this paper we describe JC's performance on unimanual conditions, as relevant to our experimental data on his monitoring and awareness of the actions of his limbs.

The CC incorporates factors known to elicit errors in everyday tasks by requiring participants to make 2 different cups of coffee (i.e., regular coffee with sugar and cream and hazelnut coffee with skim milk and sweetener) in any sequence as quickly as possible. In order to compare the performance of each hand, the task was administered as a unimanual task for both the right and the left hand. The performance of JC was compared to that of 4 right-handed control subjects—men between the ages of 48 and 60 ($M = 52.3$) and with 10 to 14 years of education ($M = 12.0$).

The task was administered as follows: 13 bimanual practice trials, during which participants received feedback on their performance and errors, were reviewed and corrected. After practice, participants performed the CC with their right or left hand on each trial. The hand that was not used was comfortably restricted in a sling. In total 12 unimanual trials were administered (in blocks of 3 trials) in an ABBA counterbalanced order.

Error analysis

Errors were coded as one of three kinds: (a) microslips, (b) detected overt errors, or (c) undetected overt errors. The first two categories denote errors that are detected. Microslips are errors in which the subject reaches towards or touches a distractor object but stops short of using it; these therefore represent episodes of correcting the erroneous movement. Overt errors include instances when an incorrect action is executed. An overt error was coded as "detected" if the participant attempted (successfully or not) to correct it or if the error was accompanied by a predetermined set of behavioural reactions to the error (i.e., distinctive manual and facial gestures: Hart, Giovannetti, Montgomery, & Schwartz, 1998). Other overt errors were coded as "undetected."

Results

Table 3 shows the total errors and the proportion from each error-detection category. JC produced more errors than did control subjects, and he required more time to complete the task: JC: R = 197.5 s, $SD = 20.3$ s; Controls: R = 88.1 s, $SD = 14.5$ s; $t(10) = 10.8$, $p < .0001$; JC: L = 209.3 s, $SD = 36.1$ s; Controls: L = 93.5 s,

Table 3. *Number of errors and proportion of errors in right- and left-hand trials for JC and controls*

		Left						*Right*					
		JC			*Controls*			*JC*			*Controls*		
Category		*M*	*SD*	*P*	*M*	*SD*	*P*	*M*	*SD*	*P*	*M*	*SD*	*P*
Detected	Microslips	6.3	2.7	0.78	1.5	0.8	0.66	4.3	1.6	0.46	1.1	0.65	0.74
	Detected, overt	0.2	0.4	0.02	0.7	0.5	0.30	3.8	1.7	0.42	0.4	0.4	0.23
	Total detected	6.5	2.7	0.80	2.2	0.8	0.96	8.1	2.8	0.88	1.5	0.7	0.97
Undetected		2.2	2.6	0.20	0.1	0.1	0.04	1.3	1.4	0.12	0.0	0.1	0.03
Total		8.7		1	2.3		1	9.4		1	1.5		1

P = proportion.

$SD = 10.4$; $t(10) = 7.6, p < .0001$. He made similar numbers of errors for trials involving his right and left hand (R = 9.4, L = 8.7; $z = -0.56$, $p = ns$), and he needed similar amounts of time ($z = -0.65, p = ns$).

There was no difference in any error type (micro-slips, overt detected, and undetected) between the hands for the normal control subjects ($z < 1.5$, $p = ns$ for all). Analysing the performance of the hands: JC showed a greater proportion of microslips with the left hand than the right hand ($z = -2.7, p < .01$) and a greater proportion of overt–detected errors with the right hand than the left ($z = -2.9$, $p < .01$). There was no right vs. left difference in overt–undetected errors ($z = -1.1$, $p = ns$).

Comment

In this task JC demonstrated different patterns of errors across both hands. He made more errors with either hand than did normal subjects. Given his left-hand callosal apraxia, errors in this naturalistic action task are not surprising (Buxbaum, Schwartz, Coslett, & Carew, 1995).

The results of the error detection analyses reveal that although JC was aware of the errors made by his right hand as often as his left (no difference in undetected errors) and that the right-hand errors were corrected later (overt–detected) than left-hand errors (microslips). At first glance, the results of this task seem at odds with our observations of JC's performance on the action-monitoring task. In that task we inferred that JC was aware of errors made by his right but not his left hand, and here we infer that he was aware of errors made by both hands. The important consistency with respect to JC's alien hand is that in both tasks he is aware of this limb's performance. The CC task as a naturalistic task is conducted at a slower pace than is the computer task, and we suspect that at this time scale JC is capable of being aware of the actions of both limbs. We interpret the fact that he was less able to control the errors of his right than his left hand as a reflection of this hand's disinhibition and its exo-evoked sensitivity.

DISCUSSION

At first glance, the alien hand syndrome is deeply puzzling. Patients observe and experience their own limbs engaged in purposeful behaviours over which they have little control. This limb may disrupt movements of the other limb that is responding to the intentions of the patient (Akelaitis, 1944–1945). Furthermore, the errant limb does not even rest during sleep (Banks et al., 1989). Our patient slept with his arm pinned against a wall to keep it from wandering and seizing things in his sleep. He, as most other patients with this syndrome, referred to this limb in the third person. Our goal in this investigation was to try to understand this sense of alienness.

From our observations, we postulate that three components are necessary to produce the alien hand syndrome in its prototypic form (which we take to be the production of actions that appear purposeful but are not intended by the patient, based on their verbal claims).[2] First, the limb must be disinhibited. Without such disinhibition, the question of abnormal movements does not arise. Second, the movements must appear purposeful. Without purpose, the question of aberrant intention does not arise. Finally, the patient must be acutely aware of the behaviour of the alien limb. Without such awareness, the experience of control by an "other" does not arise. Below, we present the evidence in support of this postulate and place our postulates in the context of other neurologic syndromes and classic and contemporary models of motor control.

Our results are consistent with the idea that JC's right hand was disinhibited. On his clinical evaluation, he clearly demonstrated continuous perseverations when drawing figures such as triple loops. In the first experiment in which a

[2] We recognize that these components may not apply to versions of the syndrome in which the primary symptom is lack of recognition of the limb, as originally described by Brion and Jedynak (1972).

stimulus directed him to respond with the right or left hand, his right hand responded more quickly and made more errors of commission than the left. Furthermore, this hand was influenced disproportionately by environmental contingencies. Its disinhibition increased disproportionately as the probability of the triggering stimuli increased. Our second experiment confirmed that JC's right hand was disinhibited and simultaneously was under less volitional control than the left. In this experiment JC was engaged in a sequential motor task. Again, his right hand responded more quickly than the left to the triggering stimulus. However, after this initial reflexive movement, it moved more slowly than the left in the subsequent movements that had to be planned on each trial. Taken together, these results show that JC's alien hand was disinhibited and his control over novel sequential movements by the right limb was impaired.

While disinhibition and loss of volitional control may be necessary, they are not sufficient to produce the alien hand syndrome. Clinical neurology is replete with examples of patients with motor disinhibition, without the reports of alienness. These examples range from simple motor tics to hemiballismus. Hemiballismus is often seen following strokes to subthalamic nuclei (Provenzale & Glass, 1995) and is characterized by dramatic large-amplitude flailing of limbs. While patients with this syndrome lose control over their limb, they do not claim that the limb is governed by an other.

We postulate that the second necessary component of the alien hand syndrome is the appearance of organized purposeful behaviour. JC found that his alien hand would reach out and seize light switches and turn them on and off repeatedly. It would also grasp his other arm when he tried to eat using his left arm. JC developed strategies to "distract" the alien limb, such as grasping a rolled-up magazine in this hand, which, he claimed, "satisfied" it. We suggest that there are two elements to JC's motor behaviour that contribute to the appearance of organized purposeful behaviour. First is the breakdown of movements into motor fragments that retain stereotypic characteristics. The idea that motor behaviour consists of stereotypic fragments can be traced to classic writings by Leipmann (as cited by Sandson & Albert, 1984, and Luria, 1966). The second is that JC's limb is driven disproportionately by external contingencies. Riddoch and colleagues (1998, 2001) emphasize this point in their experimental observations of a case with cortico-basal degeneration. Denny-Brown (1958) emphasized the interactions of endo and exo-evoked motor behaviour. JC is unable to inhibit his alien hand's movement towards objects in the environment, and the hand then produces simple motor stereotypies such as grasping or pinching. When combined with continuous perseverations, it appears that he is turning a light switch on and off. These behaviours have the appearance of purpose without actually being so. If this interpretation is correct, we predict that an alien hand would never write a letter the content of which was alien to the patient's conscious intentions, because such an act could not be performed by concatenating motor stereotypies.

While the appearance of organized purposeful behaviour of disinhibited actions may be necessary for the alien hand syndrome, it is not sufficient. Two clinical syndromes make clear that awareness of such behaviours is also critical. Patients with bilateral frontal lobe damage exhibit "utilization behaviour". Their movements may seem organized and are compelled by objects in the environment (Boccardi et al., 2002; Lhermitte, 1983). These patients are often quite demented and have little insight into what they are doing. Similarly, patients with frontal-lobe seizures may, during a seizure, engage in complex movements that give the impression of purposefulness, but they have no awareness of these movements (Ances & Chatterjee, 2003; Suwanwela & Leelacheavasit, 2002). In neither case is a subjective sense of alienness prominent.

We postulate that the third component necessary for the alien hand syndrome is that the patient be aware of what the limb is doing. Three lines of evidence suggest that our patient was acutely aware of the behaviour of his limb. First are his verbal reports. The fact that, unlike patients with utilization behaviour or frontal lobe seizures, he can describe what the limb has been doing makes this awareness self-evident. By itself, these reports do not distinguish whether he was aware of the actions as they were occurring or was simply aware of the consequence of the actions, as probably occurred in the patient described by Riddoch and colleagues (1998). Second are his reactions to his errors on the coffee challenge test. He detected the same proportion of errors with each hand. We infer that his right hand, more than his left, was driven powerfully by objects in the environment (also see Giovannetti et al., 2005, for further evidence), and after initiating an erroneous movement, he was less able to inhibit it. These observations suggest that he was aware of his errors as they were occurring, rather than representing a verbal reconstruction of earlier events. Finally, this impression is consistent with our data on his ability to monitor his actions.

Our action-monitoring task was adapted in specific ways. The basic observation is that when producing a rapid series of responses, subjects tend to be slower with a correct response that follows an error than with other correct responses (Rabbitt, 1966). The inference one makes from this observation is that subjects are aware of their errors and are cautious on subsequent trials. This observation is evident in group data of normal subjects and has been adapted to patients with focal brain damage (Gehring & Knight, 2000). Here we adapted the task even further to examine the behaviour of an individual in which the main comparison of interest is differences in performance between his right and left hands. One might object that damage to the medial frontal cortex might impair such monitoring generally, so that using these paradigms as a probe is not particularly meaningful. However, we were able to show that JC's performance on a task that does not require a limb movement (the Stroop interference paradigm) generated modulations of reaction times by errors similar to normal subjects.

Given that JC has the requisite neural machinery to generate such a behavioural effect verbally, we now turn to his behaviour on the task adapted to assess his ability to monitor the actions of each hand. Since deficits in the ability to select verbal or motor responses may dissociate with anterior cingulate damage (Turken & Swick, 1999), we cannot assume that JC would also be aware of motor errors as he was of verbal errors. Our normal subjects showed slowing of responses both during an error trial and on the trial following it. This pattern suggests that in this particular adaptation of the paradigm, subjects can monitor their error as it is happening. JC's left hand was relatively unaffected (as assessed by reaction times) by whether the trial was an error trial or the trial that followed. By contrast, his right hand was modulated by errors and was closer to the normal pattern than was the left hand. Notably, he was slower on the error trials themselves, as were our normal subjects. In addition, he was faster on the trial in which he responded correctly before the error trial. This suggests a pattern of "festination" that is sometimes seen patients with basal-ganglia disorders, where they may accelerate a movement pattern to the point of losing control. Most relevant to our claims is the fact that JC became slower on his error trials, again suggesting awareness of his erroneous movements as they were happening.

Our patient had an extensive lesion of the corpus callosum and the medial frontal cortex including the anterior cingulate gyrus. The medial frontal and dorsolateral prefrontal cortex interacts in complex ways to generate and monitor actions. Considerable evidence from monkey physiology and human studies suggests that the supplementary motor area governs internally evoked movements in planning complex actions and works in concert with the dorso-lateral prefrontal cortex, which, along with the posterior parietal regions, is responsive to environmental determinants of action (Gerloff, Corwell, Chen, Hallet, & Cohen, 1997; Goldberg, 1985; Passigham, Ramnani, & Rowe, 2004).[3]

[3] This is a variant of the classic Denny-Brown view and incorporates the dorsolateral prefrontal cortex in neural systems that mediate exo-evoked movements.

Boccardi and colleagues (2002) suggested that damage to the medial frontal cortices, especially the supplementary motor areas, might be critical to the production of utilization behaviours. Consistent with these views, our patient with medial frontal damage had more trouble with planned complex movements and was disproportionately influenced by the environment.

Gehring and Knight (2000) found that lateral prefrontal damage in patients influenced action monitoring. Specifically, they found that patients corrected a smaller proportion of errors but continued to show posterror slowing. However, the error-related negativity, which is an event-related brain potential thought to reflect medial frontal action monitoring, no longer showed the modulation based on whether the trial was correct or erroneous. The authors suggest that the dorsolateral prefrontal and medial systems modulate corrective actions but do not themselves implement them. The idea that monitoring errors and implementing their correction is distinct has theoretical support, although the neural instantiation of this distinction is controversial (MacDonald, Cohen, Stenger, & Carter, 2000). Consistent with this view, we found that medial frontal damage did not abolish JC's ability to be aware of errors being produced by his disinhibited hand.

In viewing the motor behaviour of our patient, we have drawn on classic models of motor control advocated by Denny-Brown and by Luria. Following Denny-Brown (1958), we have emphasized ideas that motor behaviour can be exo-evoked or endo-evoked and suggest that our patient's alien limb is more likely to be driven by exo-evoked contingencies. Following Luria (1966), we have conceptualized the notion of motor fragments that can be concatenated in sequential behaviours. Our observations are also relevant to contemporary models of motor control (Desmurget & Grafton, 2000; Wolpert et al., 2001).

Contemporary models of motor control incorporate both feed-forward and feedback components. Feed-forward models propose that motor commands are defined before the onset of a movement and feedback is relevant only at the very end of movement trajectories, when movements are slow. Feedback models are the conceptual opposite, positing that there is no a priori motor command. Rather, the muscle commands are generated in real time through continuous comparisons of the position of the limbs and the target. Simple feed-forward models are difficult to reconcile with observations that movements are more accurate when proprioceptive and visual information is present. Simple feedback models are difficult to reconcile with the fact that visual or proprioceptive signals need up to 100 ms to influence movements—a delay that would be ineffective since the limb is in a different position by the time these signals are available. Because of the inadequacy of these models, hybrid models have been developed in which afferent and efferent signals are integrated during movements. These models are referred to as internal models (also, in the literature, as "observer" or "sensorimotor integrator" models: Desmurget & Grafton, 2000; Wolpert et al., 2001).

These models of motor control (Blakemore, Wolpert, & Frith, 2002) assume three motor states: (a) desired state, (b) actual state, (c) predicted state. Actions are performed when goals formulate the desired state of the system. Controllers generate movement based on the differences between the actual state and the desired state and are then tuned by sensory information from the environment. The predicted state is used to estimate the future state of the system based on a forward motor program. As the actual state is available through sensory feedback only after delay, this state is critical for monitoring movements online. Adjustments are made by comparing the 3 states of the system (see Figure 9). According to this model, in alien hand syndrome the limb is disproportionately compelled by environmental stimuli (disinhibited and exo-evoked) rather than by goals. For such a movement there is no desired state and no postulation of a predicted state change; consequently, the patient is simply aware of a changing actual state. The forward component is disconnected from the feedback component. That disconnection, combined with the apparent purposefulness of the movements, and online

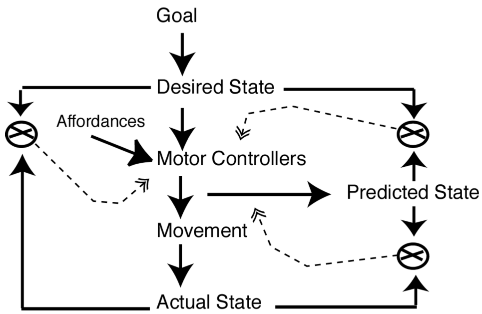

Figure 9. *Action model (adapted from Frith, Blakemore, & Wolpert, 2000).*

awareness of the movement, we postulate, produces the sense of alienness.

To summarize, we present a man with classic alien hand syndrome. This syndrome seems mysterious and would seem to offer insights into notions of self, agency, and motor control. In demystifying his behaviour using clinical and experimental observations, we suggest that three things are needed to produce this syndrome. First is a disinhibited limb that is disproportionately driven by the affordances of environmental stimuli. Second is the concatenation of motor fragments into perseverative movements that give the appearance of purpose. And third is the online awareness of the behaviour of this errant limb. The alienness is unlikely to represent a true goal-directed intention motivating the errant limb from which the patient's verbal "interpreter" system is disconnected (Cooney & Gazzaniga, 2003). Patients experience alienness in being aware of their own limb performing unintended movements that give the appearance of purpose.

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