A PET study of voluntary movement in schizophrenic patients experiencing passivity phenomena (delusions of alien control)

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Summary

Schizophrenic patients experiencing passivity phenomena believe their thoughts and actions to be those of external, or alien, entities. We wished to test the hypothesis that voluntary motor action in such patients would be associated with aberrant patterns of activation within the cerebral motor system. We used H215O PET to study patients while they performed paced joystick movements on two occasions 4–6 weeks apart. During the first scan passivity symptoms were maximal, while by the second scan these symptoms had significantly improved in five of the seven patients. Two control groups were also scanned on two occasions: deluded schizophrenic patients without passivity phenomena and normal subjects. In normal subjects, performance of freely selected joystick movements with the right hand, compared with rest, revealed relative activation of prefrontal, premotor, motor and parietal cortical regions. Schizophrenic patients with passivity showed hyperactivation of parietal and cingulate cortices. This hyperactivation remitted in those subjects in whom passivity decreased over time. This reversible hyperactivity was not a feature of schizophrenics without passivity. Given that these hyperactive cerebral regions subserve attention to internal and external bodily space, and the attribution of significance to sensory information, they provide a plausible anatomical substrate for the misattribution of internally generated acts to external entities: the cardinal feature of delusions of passivity (alien control).

Keywords: schizophrenia; passivity; delusions; PET; cerebral blood flow

Abbreviations: rCBF = regional cerebral blood flow; SPM = statistical parametric mapping

Introduction

Schizophrenia is a mental disorder characterized by abnormal beliefs, behaviours and experiences. The presence of delusions and hallucinations (in particular those of the ‘first rank’ of Schneider; see Koehler, 1979) has suggested temporal lobe dysfunction on the basis of a resemblance to the psychosis of temporal lobe epilepsy (Trimble, 1990). Recent PET blood flow studies have supported this concept (Liddle, 1987; Liddle et al., 1992).

However, few studies have examined the neural correlates of specific delusions. In one study schizophrenic and psychotic temporal lobe epilepsy patients were compared for the presence of ‘first rank’ symptoms and were alike on all classes except one: delusions of ‘passivity’ or alien control (Oyebode and Davison, 1989). This category was associated with schizophrenia alone, suggesting that brain regions other than the temporal lobe may be relevant in the genesis of these specific delusions.

Passivity delusions comprise the belief that one’s thoughts or actions are being influenced or replaced by those of an external agent (e.g. a spirit or a machine) (Mellor, 1970). When patients with passivity are compared with other schizophrenics they show impaired motor performance in the absence of visual feedback and impaired recall of their own motor acts (Frith and Done, 1989; Mlakar et al., 1994). Frith (1992) has hypothesized that such findings reflect a deficit in ‘internal monitoring’; patients do not recognize their own thoughts and actions as being internally generated and instead attribute them to alien entities.
The similarities existing between passivity and certain organic states, such as somatoparaphrenia (Critchley, 1953), have prompted suggestions that the parietal lobe and right hemisphere may be dysfunctional (Angyal, 1936; Nasrallah, 1985; Zec and Weinberger, 1986; Cutting, 1989).

Functional neuroimaging allows the neural correlates of motor control and dysfunction to be demonstrated. Normal subjects performing movements activate prefrontal, premotor, motor and association cortical regions (Playford et al., 1992), while imagined movements activate prefrontal, premotor and parietal cortex (Stephan et al., 1995). Patients with Parkinson's disease show underactivity of prefrontal and mesial premotor areas when akinetically (Jenkins et al., 1992; Playford et al., 1992) while these areas are overactive in dystonia (Ceballos-Baumann et al., 1995). In this study we have used PET to study regional cerebral blood flow (rCBF) in normal subjects and schizophrenic patients while they performed motor tasks. These motor tasks involved joystick movement and were similar to those used by Playford et al. (1992). We hypothesized that schizophrenic patients experiencing their actions as being externally controlled would exhibit abnormalities of neuronal activity (as indexed by rCBF) in cortical and subcortical regions subserving motor control.

We also wished to determine whether such abnormalities would normalize as passivity remitted and so PET was repeated 4–6 weeks later.

**Methods**

**Subjects**

We studied seven male, right-handed, schizophrenic patients, who experienced passivity phenomena. We studied them at two points in time (4–6 weeks apart); first, when they were maximally symptomatic (experiencing their actions as being under external control on the day of study), and second, when these symptoms were no longer disabling. Patients were recruited from London teaching hospitals, satisfied DSM IIIR criteria for schizophrenia (DSM, diagnostic and statistical manual of mental disorders) and had been physically investigated for the exclusion of organic cerebral pathology. None had a history of epilepsy, head injury, neurological disease, or alcohol or substance misuse. Patients were screened by consultant psychiatrists for the presence of passivity phenomena, their notes were studied, and only those with documented passivity were included. All patients scored 4 or 5 on the 'delusions of control' item in the Scale for the Assessment of Positive Symptoms (Andreasen, 1984). Those with overt movement disorders were excluded.

We also studied two control groups: (i) six schizophrenic patients (from the same psychiatric units as the index group) who were currently deluded but who did not, and had never previously, reported passivity phenomena (as supported by case note documentation of previous symptomatology); and (ii) six age-matched normal volunteers without psychiatric or neurological personal or family history. All the subjects were right handed males (assessed using the Edinburgh Handedness Inventory; Oldfield, 1971). Both control groups were scanned on two occasions. A (seventh) schizophrenic control was studied on one occasion but excluded from further analysis due to poor compliance.

Both schizophrenic groups received neuroleptic treatment for their symptoms. In neither group were there changes in oral medication within 2 weeks, or in intramuscular medication within 4 weeks, of the first scan.

All subjects underwent detailed assessment of their mental state and of any medication-related side effects prior to each scan session. Assessment included Scales for the Assessment of Positive and Negative Symptoms (Andreasen, 1983, 1984), Barnes Akathisia Scale (Barnes, 1989), Simpson and Angus Scale for Parkinsonism (Simpson and Angus, 1970), Abnormal Involuntary Movement Scale (Guy, 1976) and the Barnes Tardive Dyskinesia Scale (Barnes and Trauer, 1982). The schizophrenic groups were selected for similar neuroleptic dosage and severity of current symptomatology, with selection being biased towards those with prominent delusions (at first assessment). All patients had, therefore, pronounced 'reality distortion syndrome' (Liddle et al., 1992). Patients were also assessed using a specially devised 14-point scale, rating the presence of 'passivity' phenomena, e.g. 'made thoughts' and 'made actions'. The purpose of this scale was to derive a numerical measure of the severity of passivity phenomena (i.e. those domains currently affected: thought, affect and movement) and to assess change over time (Appendix 1).

All subjects gave informed consent to participate in the study which was approved by the ethics committees of the participating hospitals and by the Administration of Radioactive Substances Advisory Committee (ARSAC), UK.

**PET scanning**

We used PET to measure rCBF, an index of regional neuronal synaptic activity. Subjects were scanned six times in each of two sessions, 4–6 weeks apart.

We scanned all subjects under three conditions (A, B and C). Throughout, the subjects were scanned in a dark room, lying supine with their eyes closed and their head in a padded support. An auditory pacing tone was heard at a rate of once per 3 s (0.33 Hz). In the first condition (A) the subject responded by moving a joystick with their right hand in freely chosen directions. Four directions were possible and they were instructed to make sequences of movement as unpredictable (random) as possible. In the second condition (B) they moved the joystick in a stereotyped clockwise sequence (over successive moves); and in the third (C) they remained at rest. The tasks were performed in an ABCCBA sequence to control for possible order effects and habituation. Tasks A and B were similar in that they involved joystick movements in four different directions and included a working memory component: recall of the last movement made. In
the latter respect B differs from the corresponding condition used by Playford et al. (1992). However, conditions A and B differed in that A involved the free, ‘internal’ selection of movement, whereas B involved movements which were pre-specified. The scanning procedure was repeated 4–6 weeks later. Thus all subjects received a total of 12 scans (six on two occasions).

The subjects were debriefed following each scan. They were asked open questions regarding movement strategy and their thoughts during the period of scanning. Behavioural data were acquired for response selection: ‘direction’ of joystick movement, degree of ‘randomness’ during the free selection condition and response times. ‘Randomness’ was calculated using the ‘Entropy’ programme (C. D. Frith), derived from Atneave (1959), and implemented using a Macintosh computer. This program has previously been used by Frith and Done (1983).

As patients with passivity were scanned when severely symptomatic and when improving in separate sessions they acted as their own controls. Comparison with the schizophrenic group not experiencing passivity and with normal subjects controlled for possible temporal effects, repetition of procedure, and neuroleptic medication (in the patients).

rCBF was measured by recording the distribution of radioactivity in the brain after intravenous infusion of H215O, using a 953B PET scanner (CTI, Knoxville, Tenn., USA) (full width half maximum 16 mm) in three-dimensional mode with collimating septa retracted to improve sensitivity. Subjects received a 20-s intravenous bolus of H215O at a concentration of 55 MBq/ml and a flow rate of 10 ml/min through a (left) forearm cannula. Emission scanning lasted 90 s and was timed to start with the rising phase of radiotracer counts in the head (Silbersweig et al., 1993).

Image analysis

The 31 original scan slices were interpolated to 43 planes in order to render the voxels approximately cubic. All rCBF images for each subject were automatically realigned to correct for any head movement between scans (Woods et al., 1992), then transformed into standard stereotactic space corresponding to the atlas of Talairach and Tournoux (1988) with the intercommissural line as the reference plane for the transformation (Friston et al., 1989). Images were smoothed using an isotropic Gaussian kernel to increase signal-to-noise ratio and to accommodate normal variability in functional and gyral anatomy.

The data were analysed with statistical parametric mapping (SPM) (SPM 95 software from the Wellcome Department of Cognitive Neurology, London) implemented in Matlab (Mathworks, Sherborn, Mass., USA). SPM combines the general linear model (to create the statistical parametric map) and the theory of Gaussian fields to make statistical inferences about regional effects (Friston et al., 1995b). The condition, subject and covariate effects (global blood flow and neuroleptic dosage) were estimated according to the general linear model at each voxel. To test hypotheses about regionally specific condition effects, the estimates were compared using linear compounds or contrasts.

The activations associated with motor tasks presented here were generated by subtractions of the different states A, B and C, yielding areas of relatively increased and decreased rCBF. The activations seen in normal subjects provided a template for subsequent comparisons between the groups (so that subsequent analyses only interrogate those pixels belonging to the ‘normal’ motor system). Between-group comparisons assessed the significance of differences in the magnitude of activation effects across groups within the cerebral motor system. The resulting set of voxel values for each contrast constitute a statistical parametric map of the t statistic, SPMt. The SPMt were transformed to a Z distribution (SPMz) and thresholded at P < 0.001, to minimize the risk of Type 1 errors (Bailey et al., 1991).

Results

Demographic data, symptomatology and task performance

Normal subjects

The six normal males studied performed the motor tasks accurately and their response characteristics are given in Table 1. There were no significant differences between response times for freely selected (random) and externally specified (clockwise) movement. On each occasion a similar degree of ‘randomness’ was exhibited in freely selected joystick movements. Single movements were close to the theoretical score for ‘pure’ randomness (2).

Schizophrenic patients

With respect to task performance all the schizophrenic patients performed the motor task satisfactorily. Passivity patients exhibited a trend towards longer response times at the first scan session, but this failed to reach statistical significance (Table 1). They were similar to normal subjects in their ‘randomness’ measures: their responses were no more predictable (Table 1).

Passive versus non-passive schizophrenic patients

The demographic and symptomatic characteristics of the schizophrenic patients with and without passivity phenomena are given in Table 1. These groups were of similar age, premorbid verbal IQ and severity of symptomatology at their initial scan sessions. Only those with passivity phenomena achieved scores greater than zero on the passivity scale (see Appendix 1). There was no significant difference in neuroleptic dose received by either group although there was a non-significant tendency for higher doses among the passivity group (P = 0.33). Thus neuroleptic medication
normal subjects, schizophrenics, Table 1

Response characteristics and symptomatology of subjects

Table 1 Response characteristics and symptomatology of subjects

<table>
<thead>
<tr>
<th></th>
<th>Normal subjects</th>
<th>Non-passive schizophrenics</th>
<th>Passive schizophrenics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Response time (ms)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Free selection (T1)</td>
<td>650 ± 100</td>
<td>603 ± 81</td>
<td>724 ± 108</td>
</tr>
<tr>
<td>Free selection (T2)</td>
<td>577 ± 54</td>
<td>624 ± 78</td>
<td>659 ± 109</td>
</tr>
<tr>
<td>Stereotypic (T1)</td>
<td>600 ± 180</td>
<td>665 ± 165</td>
<td>680 ± 141</td>
</tr>
<tr>
<td>Stereotypic (T2)</td>
<td>580 ± 50</td>
<td>614 ± 134</td>
<td>670 ± 83</td>
</tr>
<tr>
<td>Randomnessb</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First order (T1)</td>
<td>1.988 ± 0.008</td>
<td>1.947 ± 0.042</td>
<td>1.987 ± 0.018</td>
</tr>
<tr>
<td>First order (T2)</td>
<td>1.992 ± 0.002</td>
<td>1.922 ± 0.005</td>
<td>1.995 ± 0.009</td>
</tr>
<tr>
<td>Neuroleptic doseb</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>–</td>
<td>381 ± 304</td>
<td>671 ± 439</td>
</tr>
<tr>
<td>T2</td>
<td>–</td>
<td>505 ± 248</td>
<td>678 ± 408</td>
</tr>
<tr>
<td>Delusionsc</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>–</td>
<td>2.8 ± 1.7</td>
<td>3.9 ± 0.4</td>
</tr>
<tr>
<td>T2</td>
<td>–</td>
<td>1.0 ± 1.5i</td>
<td>3.0 ± 0.8</td>
</tr>
<tr>
<td>Hallucinationsd</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>T1</td>
<td>–</td>
<td>2.5 ± 1.9</td>
<td>2.9 ± 0.7</td>
</tr>
<tr>
<td>T2</td>
<td>–</td>
<td>0.7 ± 1.6i</td>
<td>2.6 ± 1.8m</td>
</tr>
</tbody>
</table>

T1 = first scan session; T2 = second scan session, 4–6 weeks later. Data are presented as means ± SD. A index of ‘randomness’ derived from analysis of freely selected responses. A score of ‘2’ would be totally random. Analysis based upon Atneave (1959), and reported by Frith and Done (1983). BNeuroleptic dose is calculated in chlorpromazine equivalents using the conversion figures reported by Krasucki and McFarlane (1996). CSymptom scores refer to ‘global’ scores on the Scale for the Assessment of Positive Symptoms (Andreasen, 1984). DNon-passive schizophrenics demographic characteristics: mean age 37.2 ± 8.4 years; length of illness 11.6 ± 5.8 years; premorbid IQ (derived from New Adult Reading Test, Nelson and O’Connell, 1978) 103.8 ± 19.0. Edemographic characteristics of ‘passivity’ group: age 37.7 ± 9.2 years; length of illness 12.0 ± 8.6 years; premorbid IQ 107.2 ± 8.3. FPassive versus non-passive schizophrenics, t test, P = 0.051; passive schizophrenics versus normal subjects, t test, P = 0.06; non-passive schizophrenics versus normal subjects, t test, P = 0.15. GPassive versus non-passive schizophrenics, t test, P = 0.07. HPassive schizophrenics versus normal schizophrenics, t test, P = 0.35. IPassive versus non-passive schizophrenics, t test, P = 0.33. JNon-passive schizophrenics at time T1 versus non-passive schizophrenics at time T2, Wilcoxon signed-ranks test, P = 0.50. KNon-passive schizophrenics at time T1 versus non-passive schizophrenics at time T2, Wilcoxon signed-ranks test, P = 0.02. LNon-passive schizophrenics at time T1 versus non-passive schizophrenics at time T2, Wilcoxon signed-ranks test, P = 0.20. MPassive schizophrenics at time T1 versus passive schizophrenics at time T2, Wilcoxon signed-ranks test, P = 0.75. Movement disorder scale ratings were <1.0 for all groups studied.

Table 2 Passivity Scale scores in patients improving over time (n = 5)

<table>
<thead>
<tr>
<th>Patient</th>
<th>First assessment</th>
<th>Second assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>B</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>C</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>D</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>E</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Mean ±SD*</td>
<td>5.8 ± 1.9</td>
<td>3.4 ± 1.5</td>
</tr>
</tbody>
</table>

For Passivity Scale see Appendix 1. *Wilcoxon signed-ranks test, P = 0.04.

dose was entered as a possible confounding covariate in subsequent analyses of PET rCBF data.

When schizophrenic patients were assessed before the second PET scan both groups had shown improvement of their symptomatology. In those with passivity there was a significant reduction in delusions over time (Table 1), and this was accompanied by a decrease in Passivity Scale scores in five out of the seven patients (Table 2). Similarly, passivity patients reported more passivity during the first scan session than during the second (see below).

In neither schizophrenic group were there significant changes in neuroleptic medication over time (the majority of patients remained on the same dosage).

Phenomenology during PET

Five of the seven schizophrenics in the index group reported vivid experiences of passivity (alien control) while performing motor tasks during the first scan session; experiences such as ‘feeling like an automaton’, ‘guided by a female spirit who had entered me’ and ‘spirits moving my shoulder’ (Table 3). At the second session only one patient continued to report such phenomena related to movement (‘God controlling’ his movements and wishing ‘to order’ them). Those patients without passivity phenomena who reported experiences in the camera, of which there were four, mostly described auditory hallucinations (‘the whining of the machine was creating voices’, ‘the voice of someone I dislike said ‘I hate you. I hate you’”).

Motor task activations

Normal controls

Normal subjects exhibited widespread cerebral activation when performing freely-selected joystick movements relative
Table 3  Passivity patients’ subjective accounts of phenomenology during scan sessions

Phenomenology [patient; scan condition]

First scan session:
- ‘I felt like an automaton, guided by a female spirit who had entered me during it. No voice—a feeling.’ [F; stereotypic movement]
- ‘It was complicated. The voices had some kind of control over the movement.’ [F; free selection]
- ‘I thought you [the experimenter] were varying the movements with your thoughts.’ [E; free selection]
- ‘The technology purified the atmosphere. It changed the atmosphere. The spirits were moving my shoulder.’ [E; stereotypic movement]
- ‘No movement but I felt they controlled my leg’ [A; rest]
- ‘I felt a twinge in my shoulder from the spirits.’ [C; rest]
- ‘I could feel God guiding me.’ [G; free selection]

Second scan session:
- ‘God is in control of the movements...he wants me to put things into some kind of order.’ [G; free selection]
- ‘I heard a voice saying ‘okay’.’ [A; free selection]
- Visual images attributed to ‘voices’ who ‘put them in me.’ [F; rest]

Patient identities A–E relate to patient’s listed in Table 2.

Table 4  Areas of relatively increased activation in normal subjects when performing movement tasks at first scan session (relative to resting state): coordinates of maximally significant foci

<table>
<thead>
<tr>
<th>Area (Brodmann area)</th>
<th>Coordinates</th>
<th>Z-score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>x</td>
<td>y</td>
</tr>
<tr>
<td>Free selection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left PFC (9)</td>
<td>-36</td>
<td>36</td>
</tr>
<tr>
<td>Left PMC (6)</td>
<td>-52</td>
<td>4</td>
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<tr>
<td>Right PMC (6)</td>
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<tr>
<td>Left SMC (4)</td>
<td>-34</td>
<td>-40</td>
</tr>
<tr>
<td>Left SPL (7)</td>
<td>-20</td>
<td>-66</td>
</tr>
<tr>
<td>Right IPL (40)</td>
<td>40</td>
<td>-46</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>4</td>
<td>-62</td>
</tr>
<tr>
<td>Specified</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left SMC (4)</td>
<td>-28</td>
<td>-38</td>
</tr>
</tbody>
</table>

The x, y, and z coordinates refer to position within the stereotactic space according to the atlas of Talairach and Tournoux (1988). P < 0.05, corrected for multiple comparisons. Only the most significant focus is given from each area of activation (Figs 1 and 2). PFC = prefrontal cortex; PMC = premotor cortex; SMC = sensorimotor cortex; SPL = superior parietal lobule; IPL = inferior parietal lobule.

Clockwise movement, compared with rest, produced widespread activation in left sensorimotor cortex and left inferior parietal lobule on both occasions. In the first session there was also significant activation in the right inferior parietal lobule (Fig. 2). This was not seen on the second occasion (Fig. 2).

Schizophrenic patients without passivity phenomena

Once again free selection of movement was accompanied by widespread activation within cortical regions when compared with the resting state (Table 6 and Fig. 1). Deluded patients without passivity phenomena showed increased rCBF in the following regions at both sessions: bilateral premotor cortices, left sensorimotor cortex, cerebellum and bilateral superior parietal cortices. In common with the passivity group, they did not activate prefrontal regions significantly on the first occasion (Fig. 1).

Clockwise movement, compared with rest, showed activation within left sensorimotor cortex (Table 6; Fig. 2).

Changes of motor activation across time

For those ‘passivity’ patients exhibiting a reduction of passivity phenomena between the first and second scan sessions (five of the initial seven) we determined the cerebral regions showing a concomitant change in neuronal activity (Table 7). To control for temporal effects we subtracted changes in activation across time in the schizophrenic control group from those seen in the passivity group. This analysis revealed that the motor activation in the presence of greater passivity was associated with a relative hyperactivation of right inferior parietal lobule, cingulate gyrus and cerebellum during both freely chosen and clockwise movements, compared with rest (Table 7 and Fig. 3). Hypoactivation was seen in right premotor cortex and the left insula in both of these comparisons.
In both the normal and schizophrenic control groups, free selection of movement compared with rest was associated with relatively reduced activation in left superior insula in the second scan session (only at trend level in normal subjects). In addition there was relatively increased activation in normal subjects in right premotor cortex (again only at trend level) and in schizophrenic controls in cingulate gyrus, and premotor and right superior parietal cortices in the second scan session.

**Comparisons of motor activation between groups**

Three comparisons are of particular importance in this study. They are: the comparison of those passivity patients improving over time ($n = 5$), with themselves when their symptoms are reduced (reported above); the comparison of the passivity group ($n = 7$) with other schizophrenic patients (when first scanned); and the comparison of the passivity patients with the normal control group (when first scanned).

When passivity patients were compared with other schizophrenic patients at the first time of scanning they exhibited relative hyperactivation of bilateral inferior parietal lobules (Brodmann area 40), the cerebellum and foci within the cingulate gyrus during freely selected movement (Table 7). Stereotypic (clockwise) joystick movement was associated with relative hyperactivation of left premotor, right inferior parietal and cingulate cortices.

When compared with normal subjects at the first time of scanning, passivity patients exhibited relative hyperactivation of left premotor cortex, right inferior parietal lobule, right angular gyrus, and cingulate gyrus during freely selected movement. The principle area of hyperactivation during stereotypic movement was in the left premotor cortex.

Taking these comparisons together there is a consistent group of foci at which patients experiencing passivity (when
Schizophrenic passivity phenomena

Fig. 2 Brain regions showing a significantly greater neuronal response to the stereotypic (clockwise) sequence of movements with the right hand compared with rest at time T1 and in the same groups at time T2, 4–6 weeks later (A and D = normal subjects; B and E = schizophrenic controls; C and F = schizophrenics with passivity). These figures show statistical parametric maps thresholded at $P < 0.05$ (corrected for multiple comparisons). Right inferior parietal activation seen in passivity patients at time T1 (C) is not seen at time T2 (F) (see formal contrast in Table 7).

Discussion

In this study we examined the functional anatomy of motor control in schizophrenic patients who experience their acts as being under alien control. We found free selection of movement in such patients, in the presence of passivity phenomena, to be associated with relative hyperactivation of the right inferior parietal lobule (Brodmann area 40) and cingulate gyrus.

By studying these patients on two occasions, and by studying two control groups we were able to address the specific effect of diagnosis, neuroleptic medication, time effects and current symptomatology upon cerebral activation accompanying motor acts. Our data suggest that the changes described are independent of diagnosis (since they are not seen in other schizophrenics), of novelty (since they are not seen in either control group), and of neuroleptic medication (since the latter was treated as a confounding co-variante in the SPM analyses, and since the passivity patients themselves remained on similar doses of medication across time).
Table 5 Areas of relatively increased activation in ‘passivity’ patients when performing movement tasks at first scan session (relative to resting state): coordinates of maximally significant foci

<table>
<thead>
<tr>
<th>Area (Brodmann area)</th>
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<tr>
<td>Free selection</td>
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<tr>
<td>Right PMC (6)</td>
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<tr>
<td>PMC (6)</td>
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<td>Left SMC (4)</td>
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<td>Left SPL (7)</td>
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<td>Left IPL (40)</td>
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<td>Right IPL (40)</td>
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<td>ACC (32)</td>
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<tr>
<td>Right ITG (37)</td>
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<td>Cerebellum</td>
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<td>-60</td>
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<td>Specified</td>
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<tr>
<td>Left SMC/IP (4/40)</td>
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<td>-30</td>
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<tr>
<td>Right IPL (40)</td>
<td>44</td>
<td>-40</td>
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</tbody>
</table>

The x, y, and z coordinates refer to position within the stereotactic space according to the atlas of Talairach and Tournoux (1988). 

Table 6 Areas of relatively increased activation in ‘non-passive’ schizophrenic patients when performing movement tasks at first scan session (relative to resting state): coordinates of maximally significant foci

<table>
<thead>
<tr>
<th>Area (Brodmann area)</th>
<th>Coordinates</th>
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<tr>
<td>Free selection</td>
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<td>Right PMC (6)</td>
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<td>-10</td>
</tr>
<tr>
<td>Left PMC (6)</td>
<td>-22</td>
<td>-10</td>
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<tr>
<td>Left SMC (4)</td>
<td>-42</td>
<td>-32</td>
</tr>
<tr>
<td>Left SPL (7)</td>
<td>-28</td>
<td>-72</td>
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<tr>
<td>Right SPL (7)</td>
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<td>-46</td>
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<tr>
<td>Right insula/IFG (44)</td>
<td>32</td>
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</tr>
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<td>-28</td>
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<tr>
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<td>-68</td>
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<tr>
<td>Cerebellum</td>
<td>6</td>
<td>-66</td>
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The x, y, and z coordinates refer to position within the stereotactic space according to the atlas of Talairach and Tournoux (1988).

Similarly, time did not lead to similar changes in either control group, and the inclusion of the temporal effects (of the control groups) did not affect the results of the SPM analyses of the passivity group. While time as a factor has been addressed, it is worth reiterating with respect to the passivity patients studied that their rCBF abnormalities were dynamic across time (as passivity changed), suggesting that relatively static factors are unlikely to be fully explanatory (e.g. age, IQ, length of illness, diagnosis and neuroleptic exposure).

Thus, the most parsimonious explanation for the differences seen in cerebral activation between the index and control groups (and between the index group on first and second occasions) is one related to symptomatology. The passivity patients exhibited a significant improvement in their delusion
ratings across time, and this was accompanied by an improvement in their Passivity Scale scores and phenomenology reported during the scanning sessions.

**Replicability of normal activations**
The pattern of activity seen in normal subjects is consistent with that seen in previous studies, using similar methodology. But uniquely, we have shown these activations to be replicated across time. These data support the reliability and validity of the technique described, adding further weight to the significance of those changes seen in the index group across time.

**Replications of previous findings in schizophrenia**
Abnormalities of motor function in heterogeneous populations of schizophrenic patients have been found previously, using a variety of imaging modalities, but we are unaware of studies where symptomatology, medication and replication of results have been systematically addressed with regard to cerebral activation. There have been reports of attenuated sensorimotor cortex activation and lack of ‘focusing’ of activation within the motor system of schizophrenic patients which are consistent with our findings in both passive and non-passive patients (Chiarenza et al., 1985; Gunther, 1992; Guenther et al., 1994; Wenz et al., 1994; Kotrla et al., 1995; Schroder et al., 1995). It remains unclear, however, whether previous reports implicate diagnosis, symptomatology, current pharmacotherapy or the response of the schizophrenic brain to a novel paradigm. Our data suggest that in neuroleptic-treated patients such sensorimotor cortex hypoactivity is stable across time, irrespective of novelty and phenomenology (i.e. despite recovery from their delusions).

In our study, when both groups of patients were at their most symptomatic, they exhibited a relative failure of prefrontal activation during the free selection of movement...
task. Such 'hypofrontality' (failure of activation) has been repeatedly found by Weinberger and colleagues studying schizophrenic patients performing the Wisconsin Card Sort Test (a test of frontal 'executive' function; Weinberger and Berman, 1988). These authors have interpreted such dysfunction in the light of Hughlings Jackson’s concept of the 'positive' symptoms of schizophrenia (Hughlings Jackson, 1932). Positive symptoms are seen as the consequence of a failure by 'higher' brain areas to 'regulate' 'lower' centres (association cortex and subcortical regions; Hughlings Jackson, 1932; Weinberger and Berman, 1988). That the interaction of prefrontal cortex with association cortices may be abnormal in schizophrenia has received support from studies of patients performing a verbal fluency paradigm. Schizophrenic patients generating words fail to exhibit the normal pattern of frontotemporal activity (i.e. frontal activation accompanied by bilateral superior temporal 'deactivation'), which, it has been suggested, reflects a defect in 'functional connectivity' (Dolan et al., 1995; Friston et al., 1995a; Frith et al., 1995).What these studies have in common with our own is their implication of heteromodal association cortices (dorsolateral prefrontal cortex, superior temporal gyrus and inferior parietal lobule) in the pathophysiology of schizophrenia. However, where these other studies have found 'trait' related abnormalities, apparently unrelated to current symptomatology, we have described 'state' related abnormalities, temporally related to specific symptoms (of passivity). In this way our study complements those others that have attempted to 'image' the cerebral correlates of specific schizophrenic symptoms such as auditory hallucinations (McGuire et al., 1993; Silbersweig et al., 1995). Our data are, however, consistent with the Hughlings Jackson concept (offered above) in that hyperactivation of the right inferior parietal lobule and cingulate gyrus in passivity patients was co-existent with a failure of prefrontal activation (although this does not prove a failure by prefrontal cortex to ‘regulate’ these other regions).

Abnormal cerebral activations in patients experiencing passivity

Right inferior parietal lobule

Hyperactivity of the right inferior parietal region was a consistent finding in the passivity group. This region is specifically concerned with spatial programming, spatial memory, and orientation within space (Pandya and Yeterian, 1984; Roland, 1993, p. 245) and is preferentially activated by movements in extrapersonal space (Roland, 1993). It receives cortical afferents from primary and secondary sensory areas and has reciprocal cortical connections with a number of brain regions including prefrontal, premotor, cingulate and superior temporal cortices. It is an area of heteromodal association cortex.

Cingulate gyrus

The other area of hyperactivity found was the cingulate gyrus, a region subserving both executive and evaluative functions (organized anteriorly and posteriorly respectively; Vogt et al., 1992). Whereas the anterior cingulate is involved in the selection of motor and affective responses to environmental and bodily stimuli, it is believed that the posterior cingulate ‘evaluates’ sensory stimuli and is involved in mnemonic processes (Mesulam, 1981a; Pandya and Yeterian, 1984). The latter may participate in directional attention by ‘regulating the spatial distribution of expectation and by assigning impact value to motivationally relevant events’ (Mesulam, 1981a). The role of anterior cingulate in the motor response is akin to premotor regions, being maximal prior to response generation and facilitating the emergence of ‘context-relevant motor behaviours’ (Devinsky et al., 1995).

Theoretical models of passivity

Disordered ‘internal monitoring’

Frith and colleagues have reported motor abnormalities in schizophrenic patients who experience passivity: failure to correct motor errors (without visual feedback), and to remember their own motor acts (Frith and Done, 1989; Mlakar et al., 1994). Such findings are compatible with an abnormality of ‘internal monitoring’ (Frith, 1992). Our findings also support such a concept. Those brain regions found to be abnormal are those subserving the programming of, and attention to, movements in space (above). Thus, disturbed function in these regions might imbue movements with abnormal perceptual qualities. These phenomena may prompt the misattribution of such internally generated (programmed) acts to external agencies.

Alienation

Having used a motor paradigm in this study it is clear that our results may refer most appropriately to the functional correlates of motor passivity. However, it is conceivable that some elements will relate to the quality of ‘alienation’ per se, which might apply to ‘made’ thoughts or affects as much as ‘made’ movements. Previous authors have regarded the right hemisphere, and the parietal lobe in particular, as the possible origin of such ‘alienation’ (Angyal, 1936; Nasrallah, 1985; Cutting, 1989). In particular Cutting has emphasized the qualities of detachment, ‘non-belongingness’, or spatial dislocation which are common to both organic lesions of the right hemisphere and schizophrenic patients whose somatic phenomenology is lateralized (Cutting, 1989). Similar cases may be found in the classical neurological literature (as in Critchley, 1953, p. 235) and later accounts of ‘possession’ of organic aetiology. Mesulam (1981b) describes a patient with an abscess of the right parieto-occipital region who believed that his body was being controlled by external forces. He also stated: ‘my head is empty’, ‘I have no thoughts’, ‘I feel hypnotized’ (Mesulam, 1981b).

That periodic overactivity of the right parietal region (in the form of ictal phenomena) might give rise to intermittent
symptoms of alienation, is reported by Leiguarda et al. (1993). A female patient who had undergone surgical excision of a right parietal lesion subsequently developed transient episodes comprising alien limb phenomena. ‘She said: ‘Suddenly I had a strange feeling on my left side; later I could not recognize the left arm as my own; I felt it belonged to someone else and wanted to hurt me because it moved towards me . . .’” (Leiguarda et al., 1993).

Our study lends partial support for the role of the right parietal region in the aetiology of such ‘alienation’; partial because subjective alienation is not the only consequence of pathology in this region, and also because some of the clinical features of parietal lobe dysfunction (e.g. alien limbs and unilateral spatial neglect) are also found with cingulate gyrus pathology (Mesulam, 1981a; Feinberg et al., 1992). (We have not placed as much emphasis upon the cingulate findings in passivity patients in this study in view of the variable loci of the hyperactivation seen, as opposed to the circumscribed nature of the right inferior parietal lobule loci. In addition, the spatial resolution of our PET technique does not allow us to specify the lateralization of the cingulate loci as they lie close to the midline of the stereotactic space.)

Alien limb phenomena comprise one example of abnormal bodily and spatial awareness which may accompany right parietal lobe pathology. Other examples include those cases where such awareness is apparently lost (for the contralateral body and external space), as in neglect syndromes, and further, those cases in which bodily awareness is present but distorted, as with ‘phantom’ and supranumary limbs. If bodily and spatial awareness are subserved by the right parietal lobe then it is plausible that loss of neural tissue (as in infarction or excision) might lead to loss of bodily awareness (right inferior parietal lobule excision is known to result in this; Mesulam, 1981a), whereas residual tissue, which is functionally abnormal might give rise to disturbed awareness (as in the cases described above of Mesulam, 1981b; and Leiguarda et al., 1993). Phantom limbs have also been found to be associated with hyperactivation of right parietal lobe (Brodman areas 7 and 40) (Kew et al., 1994).

Our finding of reversible hyperactivation of right inferior parietal lobule is congruent with a similar distortion of awareness of self in space (rather than a loss of spatial awareness per se).

**Disordered ‘spatiality’**

In their proposed neural circuitry for spatial memory Pandya and Yeterian (1984) describe the concept of spatiality, comprising three components: bodily awareness, a spatial schema and object information. We have already made the case for passivity involving a disordered bodily awareness as a correlate of disturbed parietal (and cingulate) function. But clearly the spatial schema of such patients may be disordered if they mistake internal events for events originating outside their bodies. These authors suggest that the primate brain area 7 (in the parietal lobe) mediates outwardly oriented attention, while the cingulate mediates inwardly oriented attention (Pandya and Yeterian, 1984). Human homologues of both these regions are overactive in our passivity patients and so it is possible to argue that passivity phenomena arise as a defect of external–internal spatial schema; this concept is rather similar to that offered originally by Schneider of the disordered ego–world boundary (Koehler, 1979).

**Conclusion**

Normal subjects show a replicable pattern of cerebral activation associated with freely chosen and pre-specified voluntary motor acts. Schizophrenic patients fail to activate certain components of this motor system (prefrontal and motor areas) normally when engaging in such acts.

Patients experiencing passivity exhibit reversible hyperactivation of right inferior parietal lobule and cingulate gyrus. Both of these regions have previously been implicated in the aetiology of ‘alienation’ in organic brain disorders.

Passivity phenomena may be the phenomenological correlates of disordered functioning in the following domains: (i) the ‘internal monitoring’ of ongoing motor acts; (ii) the representation of internal and external bodily space, where such acts arise and are executed; and (iii) the salience afforded these experiences.

**Acknowledgements**

The authors wish to thank all the subjects who took part in this experiment; also Mr A. Blythe, Ms A. Williams, Mr D. Griffiths, Ms. H McDevitt and Mr G. Lewington, for their radiographical expertise; Dr S. Waikar, Dr S. MacKnight, Dr G. Anderson, Dr I. Khan, Dr R. Khan, Dr M. Constantiou and Dr S. Creasey, for technical support; Professor C. Frith, Dr S. Rajeswaran and Mr L. Schnorr, for their technical assistance; and the following for their assistance in patient recruitment: Dr M. Riccio, Dr C. Bridgett, Dr C. Bench, Dr D. James, Professor T. Barnes, Dr P. Giffuley and Dr A. Nagy. S.A.S. was supported by the Charing Cross Hospital Special Research Trustees; S.A.S., D.J.B. and P.M.G. are supported by the Medical Research Council.

**References**

Andreasen NC. Scale for the Assessment of Negative Symptoms (SANS). Iowa City: University of Iowa, 1983.


Nasrallah HA. The unintegrated right cerebral hemispheric consciousness as alien intruder: a possible mechanism for...
Schneiderian delusions in schizophrenia. Compr Psychiatry 1985; 26: 273–82.


Appendix

A scale for the assessment of passivity phenomena

This scale was devised (by S.A.S. and P.F.L.) as a means of rating the severity of passivity phenomena in those patients who were believed to experience such phenomena on the basis of their clinical reports, the reports of their consultants, and examination of their medical records.

The questions asked are similar to those used in other rating scales where passivity, or the delusion of alien control, is addressed (Wing et al., 1983; Andreasen, 1984). However we have also been mindful of the variability in the expression of such phenomena, and the existence of a potential continuum with respect to their severity (Koehler, 1979). In particular we have focused on the distinction between alien influence over internal processes (e.g. thoughts or movements) and an alien force/entity replacing those processes (e.g. in the strict definition of thought insertion, the thought belonging to an ‘Other’). This is a distinction which may have clinical importance (O’Grady, 1990), but which has been inconsistently applied in the literature (Koehler, 1979).

Thus, throughout the scale, we emphasize this distinction and score rated items accordingly. The replacement of internal processes by those of an external entity scores higher than mere influence from without. Examples are given from both our own cases and those reported in a standard account of such phenomena (Mellor, 1970).

The scale has items referring to the following domains: thought, impulses to act, actions, emotions and bodily integrity. Schizophrenic patients may report ‘made’ thoughts, impulses, actions, emotions and somatic passivity (e.g. the belief that their organs are being moved around). We include a specific item referring to hand movement as this was the area of function that we were studying most directly in the PET study described. The time frame for the scale is the preceding week.

Introduction

I’d like to ask you some questions about how your thoughts and your body have been functioning recently. Some of these questions may sound unusual, or may not apply to you, but they are a standard part of this interview. The questions refer to how you have been feeling over the last week.
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**Thoughts**

(1) Have you felt recently that your thoughts were being influenced or altered in any way? Is anyone trying to control your thinking? Do you ever wonder if you are thinking someone else’s thoughts?

If both 1 and 2 apply then score 2.

(2) Is anyone else aware of your thinking? How is this possible?

(3) Have your feelings or emotions been tampered with in any way? Is anyone able to alter them? Are your feelings your own? Do they belong to you?

(4) Is there anything wrong with your body? Has it changed in any way? Has its functions been disturbed? (Your bowels or bladder or spine?) Is any person or force responsible for this? Have any parts of your body been removed? Or replaced? Has anything been implanted?

**Examples from our data.** A number of patients described their thoughts as being influenced by external entities. A man said that 'great forces' were being used against his thinking, but that his thoughts were still his own. Another said that the thoughts were being 'pulled back' by a computer in his head. These rated as '1' on the scale.

Thought insertion was also common. One man said that thoughts were being put into his mind and that they 'felt different' from his own; another said that the television and radio were responsible for different thoughts, which were 'tampered with electrically' and always felt the same way (i.e. recognizably different from his 'own'). They rated as '2'.

(2) Is anyone else aware of your thinking? How is this possible? In what way does it happen? Is anyone able to take thoughts out of your head?

Score: 0 = symptom absent; 1 = patient believes that others are aware of his thinking through a delusional mechanism (thought broadcast); 2 = patient's thoughts have been 'taken' by external entity (thought withdrawal).

We did not have any examples of thought withdrawal, but there were cases of thought broadcast. One subject believed that psychologists at GCHQ (a government intelligence agency) were constantly monitoring his thoughts and had direct access to them. Another believed that external forces were 'tuned to his frequency' and picking up his thoughts. These scored '1'. An example of thought broadcast from the literature is a woman who said 'I am thinking about my mother, and suddenly my thoughts are sucked out of my mind by a phenological vacuum extractor, and there is nothing in my mind, it is empty . . . ' (Mellor, 1970). This account would rate '2'.

**Emotions**

(3) Have your feelings or emotions been tampered with in any way? Is anyone able to alter them? Are your feelings your own? Do they belong to you?

Score: 0 = symptom absent; 1 = emotions are influenced in a delusional way (note the mechanism described); 2 = emotions have been replaced by those of another.

The only pertinent symptom in our own patients was reported by a man who believed he was subject to 'extraterrestrial, interplanetary, radioactive forces'. These forces were 'able to' 'multiply' his anger, and he felt that they were present in the room with him. However, his emotions were his own. This rated '1'. Again Mellor provides an example of 'made' feelings which would rate a score of '2': A female patient reported, 'I cry, tears roll down my cheeks and I look unhappy, but inside I have a cold anger because they are using me in this way, and it is not me who is unhappy, but they are projecting unhappiness onto my brain. They project upon me laughter, for no reason, and you have no idea how terrible it is to laugh and look happy and know it is not you, but their emotions.' (Mellor, 1970)

**Somatic passivity**

(4) Is there anything wrong with your body? Has it changed in any way? Has its functions been disturbed? (Your bowels or bladder or spine?) Is any person or force responsible for this? Have any parts of your body been removed? Or replaced? Has anything been implanted?

(2) Is anyone else aware of your thinking? How is this possible? In what way does it happen? Is anyone able to take thoughts out of your head?

Score: 0 = symptom absent; 1 = a change in function which is due to 'influence' from without; 2 = a structural change in a body part, or its movement, removal or replacement through delusional mechanisms.

A number of subjects had symptoms referring to the body. One patient believed that he 'opened his bowels for others', and that they 'used him'. This symptom rated '1'. However when first seen he also believed that he could feel spirits twisting and moving his testicles; this was rated '2'. Another subject reported that 'they' were trying to make his organs disappear (but that his organs were still present); this rated '1'. A subject described a computer that was inserted into the left side of his brain. This rated '2'.

**Made' movements**

(5) Does anything or anyone influence your movements? Are your movements controlled by another person or force outside yourself? Does it ever seem that the movements are not your own? Or that they don't belong to you? How do you explain this? [If symptoms refer only to hand movements move to Q6, below.]

Score: 0 = symptom absent; 1 = movements under external influence (by delusional mechanism); 2 = movements have been replaced by those of another. Note mechanism described.

One man reported that a computer inserted in his brain influenced his walking. When the computer was active his gait became 'more bouncy'. This rated '1'. Another patient reported that he was used 'like a ventriloquist' (sic), in that his acts were totally controlled, and another that mis-spellings when writing were not his but those of an external agent (a spirit). These rated '2'.

**'Made' hand movements**

(6) Does anything influence or control the movement of your hands? Does any person or force use your hands without your willing it? How do you explain this?

Score: 0 = symptom absent; 1 = movements under external influence (by delusional mechanism); 2 = movements have been replaced by those of another. Note mechanism described.

A patient described trying to move his hands against 'paralysing forces'. This rated '1'. Mellor describes a patient who said: 'When I reach my hand for the comb it is my hand and arm which move, and my fingers pick up the pen, but I don't control them . . . I sit here watching them move, and they are quite independent, what
they do is nothing to do with me . . . I am just a puppet who is manipulated by cosmic strings. When the strings are pulled my body moves and I cannot prevent it.’ This would rate ‘2’.

Impulses/decisions to act
(7) Do you ever feel that the decision to do something is taken for you? Does a force that is not your own make you act in a certain way? Can you explain this? [Rated positive only if a clearly delusional entity initiates acts]

Score: 0 = symptom absent; 2 = impulse or decision to act ‘belongs to’ another entity, and is explained through a delusional mechanism.

There were no positive reports on this item in our patient group. Mellor describes a man who felt a passive impulse from without to empty a urine bottle on the ward (Mellor, 1970). He attributed the impulse to the X-ray department (‘It seemed all I could do’). This would rate ‘2’.

Analysing results
Each subject’s score (n) may be expressed out of a possible total of 14: n/14. Such a rating provides an index of the severity of passivity in two respects. Those scoring highest will be the subjects in whom passivity affects more domains of their experience (i.e. more of the seven questions are rated positive), but they will also tend to be those in whom specified functions are replaced by, rather than influenced by, external entities (i.e. higher scores on individual items). [We might represent ‘alienation’ as that proportion of n contributed by scores of ‘2’ in the above schema; where p is the number of items on which ‘2’ is scored; hence, the alienation index = 2 × (p/n).]

In this study we used only the ‘raw’ scores to assess severity of passivity in the index group of patients. With larger samples it would be possible to analyse the respective contributions of the number of domains affected, and degree of alienation, but this is inappropriate in the present context given the small sample size.