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The Role of the Prefrontal Cortex in Self-Consciousness: The Case of Auditory Hallucinations [and Discussion]

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Phil. Trans. R. Soc. Lond. B 1996 **351**, 1505-1512
doi: 10.1098/rstb.1996.0136

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The role of the prefrontal cortex in self-consciousness: the case of auditory hallucinations

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SUMMARY

Many patients with schizophrenia report hallucinations in which they hear voices talking to them or about them. Behavioural and physiological studies show that this experience is associated with processes occurring in auditory language systems associated with both the production and the reception of speech. I propose that hallucinations are experienced because patients have difficulty in distinguishing sensations caused by their own actions from those that arise from external influences. This distinction can be made by predicting the sensations that will result from executive commands (forward modelling). If the predicted sensation matches the actual sensation then no outside influences have occurred and perception of change can be 'cancelled'. At the physiological level this mechanism depends upon interactions between the prefrontal areas where the executive commands originate and posterior brain regions concerned with the resultant sensations. Evidence from functional brain imaging confirms that interactions between prefrontal (executive) areas and auditory association areas are abnormal in schizophrenia. However, this account needs to be extended before we can understand why patients experience the voices as emanating, not just from an external source, but from agents who are trying to influence their behaviour. Recent imaging studies suggest that medial prefrontal cortex is engaged when we think about other people, but the precise nature of the interaction of this brain area with other regions remains to be established.

1. THE SIGNS AND SYMPTOMS OF SCHIZOPHRENIA

The diagnosis of schizophrenia is based largely on the patient's behaviour (signs) and his self-report of his mental state (symptoms). As yet no marker has been found which can validate the diagnosis at the level of physiology. Many different patterns of signs and symptoms can lead to a diagnosis of schizophrenia, and so one patient can differ markedly from another. In addition, the severity of signs and symptoms can fluctuate and the pattern can change over time in the same patient. In these circumstances we would expect to see marked differences in the pattern of 'resting' neural activity across an unselected group of schizophrenic patients corresponding to their marked differences in mental state. This expectation has been confirmed in studies using regional cerebral blood flow (rCBF) as an index of neural activity (Liddle *et al.* 1992; Ebmeier *et al.* 1993) and there is some evidence that neural activity is more strongly related to current mental state than to diagnosis (Dolan *et al.* 1993). Given these results, I have chosen to explore the neural basis of particular symptoms rather than the pathophysiology of schizophrenia in general. An essential component of this exploration is an attempt to formulate cognitive mechanisms for the production of particular symptoms, rather than simply observing associations between symptoms and patterns of neural activity.

For the purposes of this essay, my target symptom will be auditory hallucinations. However, I shall also consider other symptoms for which similar cognitive mechanisms may be involved. Hallucinations (experiencing a percept in the absence of any external stimulus) are a common feature of schizophrenia (Sartorius *et al.* 1974) although not unique to this disorder. These hallucinations usually take the form of hearing voices (Kendell 1985) and certain particular forms, such as when the patient hears people talking about him in the third person, are considered to be especially associated with schizophrenia (Schneider 1959). Example 1 is taken from an autobiographical account of a mental breakdown that occurred well before the diagnostic criteria for schizophrenia were first put forward by Kraepelin in 1896.

Example 1.

Only a short time before I was confined to my bed I began to hear voices, at first only close to my ear, afterwards in my head, or as if one were whispering in my ear, – or in various parts of the room... These voices commanded me to do, and made me believe a number of false and terrible things.

(From John Percival Esq., *A narrative of the treatment experienced by a gentleman, during a state of mental derangement*, London, 1840).

The description of the voices in the example are typical of the descriptions given by patients today

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(Chadwick & Birchwood 1994). There are three aspects of these abnormal experiences that I shall consider in this essay.

(1)An auditory-verbal experience occurs in the absence of sensation.

(2)'Self-generated' activity is perceived to come from an external source.

(3)The voice is perceived to come from an 'agent' intending to influence the patient.

My basic thesis is that these abnormal experiences occur because of disordered interactions between prefrontal cortex and posterior brain regions.

2. WHAT IS THE NATURE OF AUDITORY HALLUCINATIONS?

Hallucinations are perceptions that occur in the absence of any sensory stimulation. Although auditory hallucinations are the most frequently reported schizophrenic patients can also experience visual, olfactory and tactile hallucinations (see table 1). However, experimental studies of hallucinations are restricted almost entirely to auditory hallucinations. Patients report that the severity of auditory hallucinations (e.g. loudness and duration) fluctuates from moment to moment. Furthermore this severity is influenced by concurrent auditory input. Margo *et al.* (1981) have shown that unstructured auditory input (such as white noise) increases the severity of hallucinations, while severity is reduced by listening to speech or music and markedly reduced by reading aloud. These results show that auditory hallucinations share resources with systems concerned with the analysis of auditory sensations.

In some cases it has been shown that what the 'voices' say closely corresponds to the content of whispers or sub-vocal speech produced by the patient (Gould 1949; see example 2). This observation suggests that auditory hallucinations may be associated with inner speech. In line with this suggestion Bick & Kinsbourne (1987) have claimed that in some patients deliberate articulation reduces the severity of hallucinations. Also David (1994) has reported one case in which the occurrence of thought broadcasting (a particular form of auditory hallucination in which the patient hears his own thoughts spoken aloud) interfered with verbal short-term memory tasks in the same manner as articulatory suppression (saying 'blah blah blah') does in normal subjects (Baddeley 1986). All these behavioural observations suggest that auditory hallucinations arise in the same systems that are engaged when people listen to external speech or generate inner speech.

Table 1. *Types of hallucination*

types of hallucination	(perception in the absence of sensation)
visual	seeing frightening faces, dwarf figures
tactile	feeling heat, being pricked, being strangled
olfactory	food is tasteless or repulsive, room smells of gas
auditory	hearing voices
	hearing one's thoughts spoken aloud (thought echo)
	voices speaking to the patient (second person hallucinations)
	voices speaking about the patient (third person hallucinations)

Example 2. Hallucinations and subvocal speech

Whisper: She knows. She's the most wicked thing in the whole wide world. The only voice I hear is hers. She knows everything. She knows everything about aviation.

Patient: I heard them say I have a knowledge of aviation.

(From Gould 1949).

Brain imaging studies confirm this conjecture at the physiological level. McGuire *et al.* (1996) have delineated the brain regions activated when normal volunteers are engaged with inner speech or imagining the sound of some one else speaking. Inner speech activates Broca's area (left inferior frontal gyrus), while imagining the sound of someone else speaking engages a number of additional areas including left premotor cortex, supplementary motor area (SMA) and left superior temporal gyrus (STG). Imaging the brain activity associated with hallucinations is difficult since the target event is involuntary and its timing cannot be predicted. Using single photon emission computerised tomography (SPECT) McGuire *et al.* (1993) observed activity in Broca's area during hallucinations and, to a lesser extent, in left STG. Cleghorn *et al.* (1992) also observed activity in left STG. Silbersweig *et al.* (1995) developed a much more sensitive technique for imaging hallucinations using positron emission tomography (PET) and observed activity in auditory association cortex. The precise location of this activity varied from patient to patient. In the extreme case of a patient who experienced visual hallucinations, the location of the activity clearly corresponded to the content of the hallucination.

All these results essentially confirm the reports of the patients. When the patients hear voices they show a similar pattern of behaviour and brain activity to those observed in normal people engaged in inner speech and/or auditory verbal imagery.

3. SELF-MONITORING

In the normal case people have no difficulty in recognizing that inner speech and auditory verbal imagery is self-generated. Thus, the first key question we have to answer about auditory hallucinations is why do the patients perceive their inner speech as coming from an external source. The ability to distinguish between self-generated images and externally caused sensations is a special case of the more general ability to attribute the source of knowledge. One example of this problem, the attribution of the source of memories, has been extensively studied in patients with various kinds of amnesia. The consensus view is that impaired source memory results from damage to the prefrontal cortex (Janowsky *et al.* 1989). The precise role of prefrontal cortex in source memory

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is not yet known. Recent brain imaging studies have shown that retrieval of items from episodic memory is associated with activity in right prefrontal cortex (Shallice *et al.* 1994). This activity seems to be associated with successful retrieval rather than the attempt to retrieve and lasts much longer (several seconds) than necessary for the successful recognition of an item presented previously. It is possible that this activity reflects the reconstruction and verification of an image of the past experience. Such reconstruction would include recovery of the source of the various components of the image.

Studies of source memory in neurological patients typically require the subject to distinguish between two external sources (list A vs list B; male voice vs female voice). In the case of hallucinations the distinction is between an external source and self-generated material. Johnson *et al.* (1993) have studied the ability of normal people to make this kind of distinction. Their results suggest that rather different processes are involved from traditional source memory. In particular such distinctions are very much easier to make.

A small number of studies of schizophrenic patients have been reported in which this kind of source memory has been studied. The results are somewhat equivocal. Bentall *et al.* (1991) asked patients either to generate category items (e.g. a fruit) or read out category items (plum). A week later they were asked to identify the source of these items (read or generated). Psychotic patients were worse than normal volunteers at this task whether or not they were hallucinating. Hallucinating patients were slightly more likely to attribute to the reading lists items they had generated themselves. Frith *et al.* (1991) asked patients to generate items in a category (e.g. animals) and then listen while the experimenter generated additional items from the same category. Ten minutes later the patient was asked to distinguish between the items he had generated and those produced by the experimenter. Once again schizophrenic patients were not good at this task, but the poor performance was related to incoherence of speech (thought disorder) rather than hallucinations.

In the experiment by Harvey (1985), patients were first asked to distinguish between words that had been read out by two different experimenters. The patients had no difficulty with this task. In the second experiment patients were shown words which they either read aloud or imagined reading aloud. Subsequently they had to distinguish between words they had read aloud and words they had imagined. Thought disordered patients were found to be bad at this task, but unfortunately the author does not report whether or not performance was related to hallucinations. Taken together these results suggest that some patients with schizophrenia do have difficulty with source memory tasks. However, the problem does not seem to relate closely to the presence of hallucinations.

There is one crucial aspect of self-monitoring in hallucinations that source memory experiments do not capture. In a source memory experiment the subject is required to make the distinction between sources sometime after the original experience. In contrast, the hallucinating patient has the immediate experience that what he is experiencing is coming from an external source when in fact it is not. This is clearly not a problem of memory.

Whenever we perform an action like speaking or moving a limb we receive sensory feed back about the consequences of this action. We can hear the sound of our own voice and we can feel the new position of our hand. In isolation this sensory information can not indicate its own source. From the feel of my hand I can not tell whether I moved it to its new position or it was moved passively by some outside force. However, studies of motor control and motor learning show that there are many other types of information from which knowledge of the source of sensation can be derived. In particular it is very likely that the brain uses 'forward modelling' to predict the consequences of action (Wolpert *et al.* 1995; see figure 1). In other words it is possible to calculate the sensory outcome of an action on the basis of the motor commands that were issued to generate that action. This information can tell us about the source of sensations. If the predicted sensory outcome does not match the observed sensory outcome then some external influence must have been at work. The information provided by forward modelling has a number of other important advantages for the performance and learning of motor skills. First, for example, errors can be detected before the arrival of the sensory feedback which indicates the consequences of the action. This is because the predictions from the forward model are available much sooner than the information from the feedback occurring after the action has been completed. The desired sensory outcome (e.g. the desired final position of the hand) can be compared with the position predicted by the forward model. If they do not match, it is likely that the wrong motor commands have been issued. These processes occur largely automatically and below the level of awareness.

I have already indicated how forward modelling allows the distinction to be made between external and internally generated influences. If the output from the forward model matches the intended outcome, but not the observed outcome then external influences must have occurred. If something went wrong with this mechanism, it might happen that mismatches between expected and observed sensory outcome would occur in the absence of external influences. In this case internally generated events could be misperceived as arising from external influences. Such misperceptions might underlie the 'Delusion of control', in which patients with schizophrenia describe feeling that their own actions are being controlled by alien forces. Forward modelling is a general strategy that can be applied to all kinds of actions and has been most extensively studied in relation to limb and eye movements. However, a failure in a forward modelling process applied to overt and covert speech could underlie auditory hallucinations. If we interpret auditory hallucinations in this way, then there are a number of other symptoms which fall into the same category (table 2). Among these are the so-called 'passivity' experiences or 'made' actions in which the patient feels that his own actions are being initiated by

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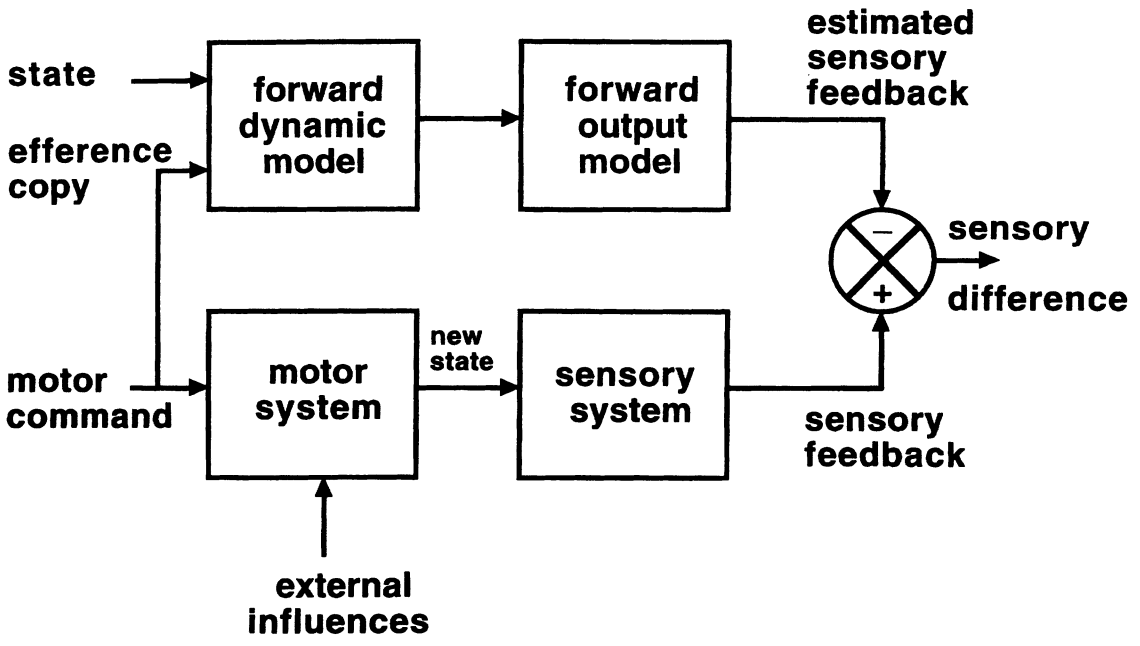

Figure 1. How do we distinguish self-generated from external sensory events? This figure shows how a 'Forward model' can predict the sensory consequences of action (estimated sensory feedback). This feedback can be used to 'Cancel out' self-generated sensory events, thus distinguishing them from sensory events with an external cause.

Table 2. *Symptoms reflecting disorders in self-monitoring*

auditory hallucinations (thought broadcasting)	'It was like my ears being blocked up and my thoughts shouted out.'
delusions of control (passivity of volition)	'My fingers pick up the pen, but I don't control them. What they do is nothing to do with me.'
thought insertion (passivity of thought)	'the thoughts of Eamon Andrews come into my mind. He treats my mind like a screen and flashed his thoughts onto it.'
(from Mellors, 1970)	

external forces. I have hypothesized that all these symptoms might be the result of something going wrong with the internal self-monitoring mechanism (maybe in the forward model) that normally permits the distinction between internally generated and external influences. As a result the patient perceives his own actions as being associated with external influences. If these patients have something wrong with the system that controls action then they should show specific types of action errors. For example, as indicated above rapid corrections of errors without feedback depends on the use of a forward model.

Two experiments suggest that schizophrenic patients do have difficulty with making rapid error corrections in the absence of visual feedback (Malenka *et al.* 1982; Frith & Done 1989). In the study by Frith & Done (1989) this difficulty was more marked in patients with passivity experiences. Mlakar *et al.* (1994) also found that such patients had difficulty subsequently recognizing designs that they had drawn in the absence of visual feedback. This would be consistent with the failure to use a forward model to construct the appearance of what had been drawn on the basis of the motor movements used. As yet there have been few investigations of this kind of control system in relation to speech. Leudar *et al.* (1992) observed the self corrections that schizophrenic patients made during the production of speech. They found that patients with hallucinations could detect their own errors as well as other patients, but found it much more difficult to self-repair them.

Clearly it will be possible to localize in the brain the various components of this model for control of action (Teuber 1964). But, as yet, we do not know where, for example, the forward model of action is computed or represented. Nor do we know in detail about the location of information about the desired or expected outcome of actions (but see Gray *et al.* 1992 for interesting speculations). Nevertheless, in broad terms the system must depend upon interactions between high level motor and sensory systems. This implies interactions between frontal/prefrontal cortex and posterior sensory association cortex. In a simple, but elegant brain imaging experiment, Paus *et al.* (1995) have shown that when subjects move their eyes in the dark at different rates, then rate related increases in activity can be seen in frontal eye fields, while rate related decreases are seen in visual areas. A similar result has been obtained by Wenzel *et al.* (1996) in relation to involuntary eye movements caused by vestibular stimulation. These results reflect a simple mechanism which permits a sensory system to discount changes in sensation due to eye movements and may correspond to the phenomenon of saccadic suppression. The same phenomenon has been observed in the somatosensory system. Elevated thresholds for per-

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ception of stimuli applied to the finger have been observed during movement of the finger (Rushton *et al.* 1981). Similar observations have also been made for the auditory system. Müller-Preuss & Ploog (1981) have found cells in the auditory cortex of the squirrel monkey which respond to the vocalizations of other monkeys, but not when the monkey itself vocalizes. Creutzfeldt *et al.* (1989) used implanted electrodes in the temporal lobes of patients undergoing neurosurgery and identified areas where the was a decrease in activity when the patient was vocalizing.

The abnormal experiences associated with schizophrenia might result from a failure of the modulation of sensory association cortex when prefrontal cortex is generating motor activity. This might be manifest as a functional disconnection between the appropriate areas, i.e. a lack of a (negative) correlation between activity in the two areas over time. Evidence for such a functional disconnection has been found in studies of schizophrenic patients performing word generation or word repetition tasks. When normal subjects perform the word generation task there is an increase in frontal and cingulate activity and a decrease in activity in the superior temporal gyrus (STG) relative to the word repetition task (Frith *et al.* 1991). This decrease was not observed in two studies of patients with schizophrenia (Frith *et al.* 1995; Dolan *et al.* 1995). Measures of functional connectivity suggest that there is a functional disconnection between frontal areas and left STG in these patients (Friston & Frith 1995).

4. THE PERCEPTION OF AGENCY

The typical hallucination described by a patient with schizophrenia is not merely a voice. It is a voice emanating from someone who is trying to influence the patient in some way (i.e. an agent). In many cases this agent is instructing the patient to perform some act which may cause violence either to the patient himself or to others. Patients expend much effort and experience much distress as they try to resist such instructions (Chadwick & Birchwood 1994). The involvement of external agents in hallucinations is a feature that puts this symptom in the same class as a large number of other symptoms common in schizophrenia (table 3). These are symptoms which involve false beliefs about agents, for instance that certain people are communicating with the patient (delusions of reference) or that people intend harm to the patient (delusions of persecution).

Table 3. *Symptoms reflecting experience of agents*

auditory hallucinations (second person)	'We won't be so lenient next time. We're going to make your eyes roll up.'
delusions of reference	'I saw someone scratching his chin which meant that I needed a shave.'
delusions of persecution	'People at work are victimising me. A bloke at work is trying to kill me with some kind of hypnosis.'

(from Chadwick & Birchwood, 1994 and Frith, 1992)

In a recent experiment we examined the effect of distorted feedback on the patients's perception of his own voice (Cahill & Frith 1996). Patients received immediate feedback of their own voice distorted in pitch. In an acute phase of the illness, but not when well, they reported that they heard another person speaking when they spoke (example 3). This willingness to attribute their own voice to another person was significantly correlated with the severity of their current delusions, but not with hallucinations. It seems that deluded patients have a strong bias to attribute unusual experiences to the actions of other agents. This tendency is often associated with hallucinations, but need not be. It seems that the tendency to attribute events to external agents is to some extent independent of the tendency to perceive inner events as coming from an external source. Thus delusional beliefs about the actions of agents can occur in the absence of hallucinations. Furthermore, when recovering from an acute episode, patients may report that they still hear the voices, but that they know they are not 'real'.

Example 3. Effects of distorted feedback

High pitch
'It only speaks when I speak. Sounds like the sound a deaf person might make'.
High pitch
'Any time I try to speak it speaks with me'.
Low pitch
'The voice has changed to a masculine voice. Same as a deaf masculine voice. I think it's an evil spirit speaking when I speak'.
(from Cahill & Frith 1996).

In this essay I use the word agent to refer to a being who acts on the basis of wishes and intentions. The recognition that other beings act on such a basis is often called 'Having a theory of mind' (Premack & Woodruff 1978). By assuming that other people have minds we are able to predict and control their behaviour on the basis of their knowledge and beliefs. Intensive research suggests that humans have a highly developed theory of mind, while other primates have this in a most rudimentary form, if at all (Cheney & Seyfarth 1990). Deluded patients seem to have an over active theory of mind. They perceive intentions when none are present and sometimes attribute intentions to inanimate objects.

The acid test of having a theory of mind is the ability to handle false beliefs (Wimmer & Perner 1983). We can recognize that a person will act on the basis of a belief even when we know that this belief is incorrect. This is not possible for children under about four years of age or for most people with autism. A good example of their problem involves lying. Lying is a strategy for manipulating the behaviour of others by instilling in them a false belief. Young children and people with autism fail to use the strategy of lying (Sodian & Frith 1992). Preliminary results with schizophrenic patients suggest that they may also have difficulty with tasks

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Table 4. *Activity in medial frontal cortex (BA8)*

Study	condition	coordinates *x*	*y*	*z*
Fletcher *et al.* 1995	theory of mind	−12	42	36
Wise *et al.* (see text)	computer vs human speech	−6	40	36
McGuire *et al.* 1996	alien vs distorted speech	−2	36	36
McGuire *et al.* 1995	auditory imagery, low in hallucinators	−12	44	36
Silbersweig *et al.* 1995	during hallucinations	−2	35	39

which involve inferring the mental states of others (Corcoran *et al.* 1995; Frith & Corcoran 1996).

The observation that people with autism can be otherwise quite intelligent, but still not be able to handle false belief tasks suggests that there may be a fairly circumscribed neural system for having a theory of mind which can be damaged while the rest of the brain remains intact (U. Frith *et al.* 1991). We have explored this possibility by imaging brain activity while normal volunteers read stories in which the behaviour of the characters can only be understood on the basis of their intentions and beliefs about the situation described. When compared with control stories in which the mental states of the characters are irrelevant we observed an area of activation in the medial prefrontal cortex on the left (Brodmann area 8) which only appeared during the mental state stories (Fletcher *et al.* 1995). A similar result has been obtained in a French study where volunteers simply listened to stories (Mazoyer *et al.* 1993).

Since animals other than man do not seem to be able to perform false belief tasks we have little relevant information from lesions studies or single cell recordings. It is therefore hardly surprising that we know little about this medial frontal area in terms of its function or its connections with other areas. However, activity has been observed in this area in a number of relevant PET studies (table 4). Wise and his colleagues (personal communication) observed activity in this area during performance of a task in which normal subjects had to distinguish between speech sounds and similar computer generated sounds. Such a task can be interpreted as requiring the detection of agents (humans) from among non-agents (computers). This area was also implicated in two studies directly concerned with hallucinations. Silbersweig *et al.* (1995) observed the activity associated with hallucinations in an untreated schizophrenic patient. This patient experienced combined auditory and visual hallucinations in which rolling, disembodied heads spoke to him, giving instructions. Activity associated with these experiences was observed in a number of areas including a medial frontal area close to that observed In the 'Theory of mind' study (see table 4). McGuire *et al.* (1995) studied auditory-verbal imagery in schizophrenic patients who experience hallucinations when ill, but who were symptom free at the time of testing. These patients showed significantly less activity in this medial frontal area than control subjects when they were imagining the sound of someone speaking. Taken together, these results suggest that a) the medial prefrontal area has a role in tasks which involve detecting and dealing with agents and b) that this area is implicated in hallucinations. The precise interpretation of the results is not easy since we know so little about either the cognitive mechanisms underlying agency detection tasks or about the function and anatomy of this area of prefrontal cortex.

The problems associated with interacting with agents (i.e. predicting and influencing the behaviour of other people) are conceptually very similar to those associated with the control of our own actions. In the control of action forward modelling can be used to predict the new state (sensations and perceptions) that will result from an action. When interacting with an agent, forward modelling could be used in the same way to predict the effect of our action on the inner state of the other person rather than ourselves. Likewise, just as we can use an inverse model to compute the executive commands necessary to reach a desired state for ourselves, we could use an inverse model to work out what sort of behaviour on our part would produce the desired state in another.

At present we know rather little about how forward and inverse models are implemented in the brain during the control of action, and almost nothing about the mechanisms that allow us to interact with other people. There is clearly an important role for medial prefrontal areas in interactions with others, but these areas must be part of an extended system yet to be identified. The phenomenology of auditory hallucinations suggest that the two systems (controlling actions of the self and controlling interactions with others) are related although not identical. Hallucinations (perception in the absence of sensation) and delusions about influences from other people are usually, but not always associated. The observations that hallucinations and delusions fluctuate markedly over time and are influenced by drugs implies that the problem arises in the dynamics of interactions between brain regions rather than some more static structural abnormality. This dynamic interaction undoubtedly involves prefrontal cortex, but the details of the system are yet to be determined.

REFERENCES

Baddeley, A. 1986 *Working memory*. Oxford: Oxford University Press.

Bentall, R. P., Baker, G. A. & Havers, S. 1991 Reality monitoring and psychotic hallucinations. *Br. J. Clin. Psychol.* **30**, 213–222.

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Bick, P. A. & Kinsbourne, M. 1987 Auditory hallucinations and subvocal speech in schizophrenic patients. *Am. J. Psychiat.* **144**, 222–225.

Cahill, C. & Frith, C. D. 1996 False perceptions or false beliefs? Hallucinations and delusions in schizophrenia. In *Case studies in cognitive neuropsychiatry* (ed. J. C.Marshall & P. Halligan), Hove: Erlbaum (UK) Taylor & Francis (In the press).

Chadwick, P. & Birchwood, M. 1994 The omnipotence of voices. A cognitive approach to auditory hallucinations. *Br. J. Psychiat.* **164**, 190–201.

Cheney, D. L. & Seyfarth, R. M. 1990 *How monkeys see the world.* Chicago: Chicago University Press.

Cleghorn, J. M., Franco, S., Szetchtman, B., Kaplan, R. D., Szetchtman, H., Brown, G. M., Nahmias, C. & Garnett, E. S. 1992 Towards a brain map of auditory hallucinations. *Am. J. Psychiat.* **149**, 1062–1069.

Corcoran, R., Mercer, G. & Frith, C. D. 1995 Schizophrenia, symptomatology and social inference: Investigating 'Theory of mind' in people with schizophrenia. *Schiz. Res.* **17**, 5–13.

Creutzfeldt, O., Ojeman, G. & Lettich, E. 1989 Neuronal activity in the human lateral temporal lobe II. Responses to the subject's own voice. *Exp. Brain. Res.* **77**, 476–489.

David, A. S. 1994 The neuropsychological origin of auditory hallucinations. In: *Neuropsychology of schizophrenia* (ed. A. S. David & J. Cutting), pp. 269–313. Hove: Lawrence Erlbaum Associates.

Dolan, R. J., Bench, C. J., Liddle, P. F., Friston, K. J., Frith, C. D., Grasby, P. M. & Frackowiak, R. S. J. 1993 Dorsolateral prefrontal cortex dysfunction in the major psychoses: symptom or disease specificity? *J. Neurol. Neursurg. Psychiat.* **56**, 1290–1294.

Dolan, R. J., Fletcher, P., Frith, C. D., Friston, K. J., Frackowiak, R. S. J. & Grasby, P. M. 1995 Dopaminergic modulation of impaired cognitive activation in the anterior cingulate cortex in schizophrenia. *Nature, Lond.* **378**, 180–182.

Ebmeier, K. P., Blackwood, D. H., Murray, C., Souza, V., Walker, M., Dougall, N., Moffoot, A. P., O'Carroll, R. E. & Goodwin, G. M. 1993 Single-photon emission computed tomography with 99mTc-exametazime in unmedicated schizophrenic patients. *Biol. Psychiat.* **33**, 487–95

Fletcher, P., Happé, F., Frith, U., Baker, S. C., Dolan, D. J., Frackowiak, R. S. J. & Frith, C. D. 1995 Other minds in the brain: a functional imaging study of "theory of mind" in stody comprehension. *Cognition* **57**, 109–128.

Friston, K. J. & Frith, C. D. 1995 Schizophrenia: A Disconnection Syndrome? *Clin. Neurosci.* **3**, 89–97.

Frith, C. D. 1992 *The cognitive neuropsychology of schizophrenia.* Hove: Lawrence Erlbaum.

Frith, C. D. & Corcoran, R. 1996 Exploring 'theory of mind' in people with schizophrenia. 1996 *Psychol. Med.* **26**, 521–530.

Frith, C. D. and Done, D. J. 1989 Experiences of alien control in schizophrenia reflect a disorder in the central monitoring of action. *Psychol. Med.* **19**, 359–363.

Frith, C. D., Friston, K. J., Herold, S., Silbersweig, D., Fletcher, P., Cahill, C., Dolan, R. J., Frackowiak, R. S. J. & Liddle, P. F. 1995 Regional brain activity in chronic schizophrenic patients during the performance of a verbal fluency task. *Br. J. Psychiat.* **167**, 343y349.

Frith, C. D., Friston, K. J., Liddle, P. F. & Frackowiak, R. S. J. 1991 Willed action and the prefrontal cortex in man: a study with PET. *Proc. R. Soc. Lond.* B **244**, 241–246.

Frith, C. D., Leary, J., Cahill, C. & Johnstone, E. C. 1991 Disabilities and circumstances of schizophrenic patients – a follow-up study. IV.Performance on psychological tests: demographic and clinical correlates of the results of these tests. *Br.J. Psychiat.* **159**, (suppl. 13), 26–29.

Frith, U., Morton, J. & Leslie, A. M. 1991 The cognitive basis of a biological disorder: autism. *TINS* **38**.

Gould, L. N. 1949 Auditory hallucinations and subvocal speech. *J. Nerv. M. Dis.* **109**, 418–427.

Gray, J., Feldon, J., Rawlins, J., Hemsley, D. & Smith, A. 1991 The neuropsychology of schizophrenia. *Behav. Brain. Sci.* **14**, 1–84.

Harvey, P. D. 1985 Reality monitoring in mania and schizophrenia. *J. Nerv. Ment. Dis.* **173**, 67–73.

Janowsky, J. S., Shimamura, A. P. & Squire, L. R. 1989 Source memory impairment in patients with frontal lobe lesions. *Neuropsychologia* **27**, 1043–1056.

Johnson, M. K., Hashtroudi, S. & Lindsay, D. S. 1993 Source monitoring. *Psychol. Bull.* **114**, 3–28.

Kendell, R. E. 1985 Schizophrenia: clinical features. In *Psychiatry*, vol. 1 (ed. R. Michels & J. O. Cavenar), p.8. Basic Books: London.

Leudar, I., Thomas, P. & Johnson, M. 1992 Self-repair in dialogue and schizophrenics: effects of hallucinations and negative symptoms. *Brain Lang.* **43**, 478–511.

Liddle, P. F., Friston, K. J., Frith, C. D., Hirsch, S. R., Jones, T. & Frackowiak, R. S. J. 1992 Patterns of cerebral blood flow in schizophrenia. *Br. J. Psychiat.* **160**, 179–186.

Malenka, R. C., Angel, R. W., Hampton, B. & Berger, P. A. 1982 Impaired central error correcting behaviour in schizophrenia. *Arch. Gen. Psychiat.* **39**, 101–107.

Margo, A., Hemsley, D. R. & Slade, P. D. 1981 The effects of varying auditory input on schizophrenic hallucinations. *Br. J. Psychiat* **139**, 122–127.

Mazoyer, B. M., Tzourio, N., Frak, V., Syrota, A., Murayama, N., Levrier, O., Salamon, G., Dehaene, S., Cohen, L. & Mehler, J. 1993 The cortical representation of speech. *J. Cog. Neurosci.* **5**, 467–479.

McGuire, P. K., Shah, P. and Murray, R. M. 1993 Increased blood flow in Broca's area during auditory hallucinations in schizophrenia. *Lancet* **342**, 703–706.

McGuire, P. K., Silbersweig, D. A., Wright, I., Murray, R. M., David, A. S., Frackowiak, R. S. J. & Frith, C. D. 1995 Abnormal inner speech: a physiological basis for auditory hallucinations. *Lancet* **346**, 596–600.

McGuire, P. K., Silbersweig, D. A., Murray, R. M., David, A. S., Frackowiak, R. S. J. & Frith, C. D. 1996 Functional anatomy of inner speech and auditory verbal imagery. *Psychol. Med.* **26**, 29–38.

Mellors, C. S. 1970 First-rank symptoms of schizophrenia. *Br. J. Psychiat.* **117**, 15–23.

Mlakar, J., Jensterle, J. & Frith, C. D. 1994 Central monitoring deficiency and schizophrenic symptoms. *Psychol. Med.* **24**, 557–564.

Müller-Preuss, P. & Ploog, D. 1981 Inhibition of auditory cortical neurones during phonation. *Brain Res.* **215**, 61–76.

Nathaniel-James, D. & Frith, C. D. 1996 Confabulation in schizophrenia: evidence of a new form? *Psychol. Med.* **26**, 391–399.

Paus, T., Marrett, S., Evans, A. C. & Worsley, K. 1995 Neurophysiology of saccadic suppression in the human brain. *4th IBRO World Congress of Neuroscience* **478**.

Premack, D. & Woodruff, G. 1978 Does the chimpanzee have a theory of mind? *Behav. Brain Sci.* **4**, 515–526.

Rushton, D. N., Rothwell, J. C. & Craggs, M. D. 1981 Gating of somatosensory evoked potentials during differnt kinds of movement in man. *Brain* **104**, 465–491.

Sartorius, N., Shapiro, R. & Jablensky, A. 1974 The international pilot study of schizophrenia. *Schiz. Bull.* **1**, 21–35.

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Schneider, K. 1959 *Clinical psychopathology*. New York: Grune & Stratton.

Shallice, T., Fletcher, P., Frith, C. D., Grasby, P., Frackowiak, R. S. J. & Dolan, R. J. 1994 Brain regions associated with acquisition and retrieval of verbal episodic memory. *Nature, Lond.* **368**, 633–635.

Silbersweig, D. A., Stern, E., Frith, C. D., Cahill, C., Holmes, A., Grootoonk, S., Seaward, J., McKenna, P., Chua, S. E., Schnorr, L., Jones, T. & Frackowiak, R. S. J. 1995 A functional neuroanatomy of hallucinations in schizophrenia. *Nature, Lond.* **378**, 176–179.

Sodian, B. & Frith, U. 1992 Deception and sabotage in autistic and normal children. *J. Child Psychol. Psychiat.* **33**, 591–605.

Teuber, H-L. 1964 The Riddle of Frontal Lobe Function in Man. In *The frontal granular cortex and behavior* (ed. J. M. Warren & K. Akert), pp. 410–444. New York: McGraw-Hill.

Wenzel, R., Bartenstein, P., Dieterich, M., Danek, A., Weindl, A., Minoshima, S., Ziegler, S., Schwaiger, M. & Brandt, Th. 1996 Deactivations of human visual cortex during involuntary ocular oscillations. *Brain* **119**, 101–110.

Wimmer, H. & Perner, J. 1983 Beliefs about beliefs: representation and constraining function of wrong beliefs in young children's understanding of deception. *Cognition* **21**, 103–128.

Wolpert, D. M., Ghahramani, Z. & Jordan, M. I. 1995 An internal model for sensory motor integration. *Science* **269**, 1880–1882.

Discussion

A. Lawrence (*Department of Experimental Psychology, University of Cambridge, Downing Street, Cambridge CB2 3EB, U.K.*). Your pet activation study revealed a focal change in rcbf in the 'Theory of mind' condition, which might imply the existence of a specific 'Theory of mind' module. However, using a somewhat different mentalising task – in which subjects had to draw inferences based on other people's knowledge, states and beliefs, Grafman and colleagues found activation of a much more distributed neural network, encompassing left front medial lobe (area 9) and left temporal lobe (areas 21, 38 and 39), which would imply that a far more distributed neural network was involved in this particular mentalizing task. In the light of these results, is it your view that the ability to have a 'Theory of mind' is a unitary (i.e. modular) ability or are different cognitive processes required for performing different 'Theory of mind' tasks?

C. Frith. The activity observed by Grafman and his colleagues (-12, 38, 32; Goel *et al.* 1996, *Neuroreport* **6**, 1741–1746) in the medial frontal lobe is within a few millimetres of the area of peak activity in our study (−10, 40, 36). However, as you say, activity in a number of other areas was also observed. I am sure that the performance of any 'Theory of mind' task will depend on the integration of activity in many brain areas reflecting the combination of many cognitive processes. By subtracting appropriate control tasks we can try to identify these different cognitive processes. I suspect that the more distributed activity observed by Goel *et al.* reflects differences in the nature of the control tasks as much as their mentalizing task. In our study the experimental and control tasks (mental and physical stories) differed on very few parameters. It will be interesting to see whether performance of many different kinds of 'Theory of mind' tasks is associated with activity in a small number of key areas. I believe that there is a key 'Modular' process that is essential to the performance of all 'Theory of mind' tasks, but I am not yet able to define this process in cognitive terms.

D. Weinberger (*Clinical Brain Disorders Branch, National Institute of Mental Health, Neuroscience Center at St. Elizabeths, 2700 Martin Luther King Jr, Ave, SE, Washington, D.C. 20032, U.S.A.*). There is an extensive literature on 'Theory of mind' as a basis for trying to understand autism. Have you looked at the performance of schizophrenics on any of the tasks used to study the theory of mind?

C. Frith. My colleague, Rhiannon Corcoran has carried out a series of studies in which schizophrenic patients performed various 'Theory of mind' tasks, some of which were derived from the autism literature (Corcoran *et al.* 1995, *Schizophrenia Research* **17**, 5–13; Frith & Corcoran 1996, *Psychological Medicine* **26**, 521–530). The results of these studies suggest that patients with negative features perform worse on 'Theory of mind' tasks than would be expected on the basis of their current IQs. There is also some evidence, though less strong, that patients with delusions about the intentions of other people (e.g. delusions of persecution and delusions of reference) perform 'Theory of mind' tasks badly. Patients currently in remission have no problems with the tasks suggesting that this is a state, rather than a trait variable.

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