

Neuropsychology of schizophrenia

What are the implications of intellectual and experiential abnormalities for the neurobiology of schizophrenia?

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The diagnosis of schizophrenia is largely based on reports of bizarre experiences such as having alien thoughts inserted into one's mind. Many patients with this diagnosis show a marked intellectual decline and particular problems with tasks involving certain kinds of memory or requiring mental flexibility. Similar patterns of performance can be seen in patients with damage in the prefrontal cortex. However, patients with schizophrenia show a very varied pattern of impairments relating to their current mental state. Chronic patients with negative features, such as poverty of speech, are most likely to show poor test performance, while the presence of severe hallucinations and delusions need not be associated with any impairment. A cognitive approach suggests that hallucinations and delusions result from the patient attributing his own actions to an external agency. This error is due to an inability to distinguish between external events and perceptual changes caused by his own actions. The basis of this failure could be a functional disconnection between frontal brain areas concerned with action and posterior areas concerned with perception.

In the continued absence of a biological marker for schizophrenia, the diagnosis is made on the basis of signs and symptoms and remains, to a certain degree, arbitrary. Currently, the most widely used definition is to be found in the diagnostic manual of the American Psychiatric Association (DSM-IV). In cases diagnosed by this scheme, most patients will have reported bizarre delusions (e.g. thought broadcasting; thoughts leave the patient's mind and enter the minds of others) and/or prominent hallucinations of a voice (e.g. voices discussing the patient's actions). In addition, these experiences will have been prolonged rather than transient. The symptoms must have been present for at least a week and there must have been signs of a more general disturbance for at least 6 months. The majority of patients receiving a diagnosis of schizophrenia never fully recover¹. The typical 'chronic' patient will manifest abnormal behaviour best characterised as lacking volition; poverty of speech, poverty of movement and poverty of ideas. Such patients may not report hallucinations or delusions, but the vast majority will have experienced

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these at some time in the course of their illness. Confronted with such cases, the challenge for the neuropsychologist is to provide data from observations and experiments which give clues to the nature of the brain dysfunctions which underlie the signs and symptoms associated with schizophrenia. There are two fundamental approaches. The descriptive approach asks the question, is there a characteristic pattern of intellectual impairment associated with the diagnosis of schizophrenia? The mechanistic approach asks the question, what psychological processes give rise to particular signs and symptoms associated with schizophrenia and how do these processes relate to normal brain functioning?

The pattern of intellectual impairments

General decline

When Kraepelin used the term *Dementia Praecox* to label what we now call schizophrenia, he was emphasising his observation that such patients often show a dramatic and irreversible decline in intellectual function shortly after the onset of their illness in early adulthood. A number of recent studies confirm this observation. Johnstone and her colleagues¹ attempted to trace all the people in the Harrow Health District who had been discharged with a diagnosis of schizophrenia during a 10 year period. Intellectual functioning was assessed in 283 cases. An estimate of premorbid functioning showed no difference from controls, but current IQ was, on average, 16 points lower². A similar result was obtained by Nelson and her colleagues³ in a group of chronic patients. These observations confirm the reports of many earlier studies⁴ showing that intellectual functioning is impaired in schizophrenic patients. While there may be some patients who were always impaired⁵, the evidence for a decline in function is striking. It is not clear how rapidly this decline occurs. It seems to be complete within 5 years of onset of the illness, but may well start before the first psychotic symptoms appear.

Specific impairments

If the brain abnormalities associated with schizophrenia are restricted to certain areas or systems, then we would expect to find that intellectual impairment was more marked in some domains than others. There have been many studies in which batteries of neuropsychological tests have been used to assess schizophrenic patients in the hope of demonstrating a characteristic pattern of impaired and spared functions. A major problem

with these (and in indeed all) studies of schizophrenia arises from the fact that the vast majority of patients are on large and chronic amounts of medication. Surprisingly, almost nothing is known about the effects of these drugs upon test performance. Saykin and his colleagues⁶ overcame this problem by studying chronic patients who were drug free at the time of testing. Even in this drug free population, the average performance of the group was at least one standard deviation below the normal level in all the ten domains that were examined confirming the existence of a general intellectual decline. However, in three domains, all concerned with learning and memory, performance was substantially worse. Although these results are clear cut in terms of test performance, the implications for underlying brain dysfunction are far less certain. The authors conclude that the specific impairments in memory and learning are consistent with damage in medial temporal cortex. However, there are many different varieties of learning and memory, each associated with different brain systems⁷. As a measure of verbal memory, Saykin and colleagues used story recall. The same task was used by Shallice and his colleagues⁸ in an intensive study of a small group of patients. These patients also performed very badly on story recall, but many of the same patients performed within the normal range on a test of forced choice recognition of words. Since performance of this latter task is impaired by temporal lobe lesions, Shallice and colleagues concluded that, if there was any specific impairment in schizophrenic patients, this was consistent with frontal rather than temporal damage. A number of other studies have applied batteries of tests to schizophrenic patients in order to identify a specific domain of impairment. As Table 1 shows, the results are not fully consistent since each study tends to implicate a slightly different domain.

Cognitive impairments

One reason for these problems is that no psychological test is 'pure'. Many different underlying processes are necessary for good test performance. If there is a circumscribed domain of impairment associated with schizophrenia this will best be described in 'cognitive', rather than behavioural, terms. Cognitive processes, such as selective attention,

Table 1 Specific neuropsychological impairments in schizophrenia

Kolb & Wishaw ¹⁰	'Frontal and temporal lobe' tasks
Saykin <i>et al.</i> ⁶	Memory and learning
McKenna <i>et al.</i> ⁹	Semantic memory
Shallice <i>et al.</i> ⁸	Executive tasks
Shoqeirat & Mayes ¹¹	Effortful tasks

planning and episodic memory, exist at the interface between behaviour and brain function. The cognitive impairments have to be inferred from the pattern of test performance or, better still, from performance on experimental tasks designed to test specific hypotheses.

Abnormal semantic categorisation

Performance on standardised tests is an obvious starting point for making hypotheses about underlying cognitive impairments. Following observations of specific problems with semantic memory⁹, Chen and his colleagues¹² used an ingenious technique to examine the boundaries of semantic categories. Subjects were asked whether items such as robin, penguin, aeroplane or bell were examples of the category *birds*. When the time to make such a categorisation is measured in normal volunteers, items clearly in the category (robin) or clearly outside the category (bell) are associated with rapid decisions, while items on the boundary (penguin) are associated with slow decisions. In terms of these decisions times, schizophrenic patients have enlarged semantic categories. They showed the slowest responses for items just outside the category such as aeroplane. Categories such as 'birds' are imposed 'top down' in order to perform the task. We could easily switch to a new category, such as *things that fly*, which would give a different ordering of the items listed above. In terms of such a 'top down' categorisation process, we could hypothesise that abnormally enlarged categories result from an impairment in some kind of 'surround inhibition' function so that items on the edge or just outside the category are not sufficiently inhibited. Results consistent with this idea have been obtained in other studies using very different paradigms^{13,14}.

Perseveration

Elliot and her colleagues¹⁵ examined the abnormal behaviour displayed by many schizophrenic patients on tasks such as the Wisconsin card sorting test. In this task, subjects must learn to sort cards on the basis of one of various features such as colour and shape. Once the subject has learned that colour is relevant and shape irrelevant, the rule is changed. The subject must now shift to a new feature and attend to something that was previously irrelevant. Elliot and her colleagues argue that there are two independent reasons for failing to switch in such a situation: (i) the subject can not stop responding to the old feature (perseveration); and (ii) the subject can not switch attention to a feature that was previously

irrelevant (learned irrelevance). Using an experimental paradigm which distinguished between these two possibilities, it was shown that the problem lay in continued responding to the old feature and not in switching attention to a previously irrelevant feature. At present, it is not clear to me whether this deficit in attention can be related to the problem with semantic boundaries demonstrated by Chen and colleagues¹². This might be because the unifying concept has yet to be delineated, but another possibility is that different cognitive impairments are found in different patients.

Intellectual impairments and schizophrenic syndromes

At any one time, an unselected group of schizophrenic patients will differ widely in their current mental state. An individual patient might be experiencing extreme and continuous hallucinations and delusions, she might manifest negative features and social withdrawal or she might be functioning relatively normally. It would seem likely that these states would be associated with very different patterns of performance on psychological tests. A number of studies (see also chapter by Liddle) have found evidence that three clusters of signs and symptoms are sufficient to capture the current mental state of most patients¹⁶. These are *Psychomotor Poverty* (poverty of speech, action and thought), *Disorganisation* (incoherence of speech and incongruity of affect) and *Reality Distortion* (hallucinations and delusions). These clusters are associated with different patterns of test performance. In the large study reported by Frith and his colleagues², general cognitive impairment was associated with poverty and disorganisation, but not with reality distortion. However, the pattern of impairment differed between the poverty and the disorganised syndrome. Poverty was associated with omission errors: poor verbal fluency, ignored signals in a vigilance task, while disorganisation was associated with commission errors; odd words in verbal fluency, inappropriate responses in the vigilance task. Similar results have been obtained in other studies (see Table 2).

Table 2 Cognitive impairments and the signs and symptoms of schizophrenia

Hallucinations and delusions	Disorganised behaviour	Negative features
—	Decline in IQ ²	Decline in IQ ^{2,3}
—	Odd verbal fluency ^{2,17}	—
—	—	Poor verbal fluency ^{2,17}
—	Commission errors ²	—
—	—	Omission errors ²
—	Stroop interference ¹⁸	—
—	—	Stereotyped behaviour ¹⁹

However, the relationship between specific impairments and current symptoms is by no means strong. For example, with the semantic anomalies discussed in the previous section, Spitzer and colleagues¹³ found them to be related to formal thought disorder, Beech and colleagues¹⁴ found them related to positive symptoms and Chen and colleagues¹² did not find them to be related to any aspect of current state. In the study of Frith and colleagues², there were clear cut relationships, but the number of cases was very large (283). A power calculation suggests that equivalent relationships would not be reliably detected in studies involving less than ~50 cases.

If cognitive impairments are closely associated with current mental state, then a strong prediction would be that these impairments should change with changes in mental state. This should be a particularly sensitive measure, since noise due to differences between patients would be eliminated. Such studies are difficult to carry out, however, especially as they could be confounded by changes in drug treatment. It is of interest that Goldberg and his colleagues²⁰ found that general cognitive impairments remained even after symptoms had been substantially reduced by treatment with clozapine.

Cognitive mechanisms underlying specific symptoms

All the studies described above are correlational. They address the question of whether schizophrenia or certain signs and symptoms are associated with certain cognitive impairments. As is well known, such studies can not address questions of causation and will always be unsatisfactory since an apparent link may be spurious, being mediated by some hidden factor. There is a sense in which schizophrenia will never be satisfactorily 'explained' in terms of cognitive impairments. Nor can an explanation solely in terms of a gene or a particular form of brain abnormality be considered satisfactory. In contrast, it is possible to 'explain' particular signs or symptoms in cognitive terms¹⁹ and then link these to brain abnormalities. Such an explanation involves the description of a cognitive mechanism that causes the symptom of interest. On the basis of such a description, it should be possible to: (i) design experiments that reveal the functioning of the relevant cognitive mechanism; (ii) devise procedures which alter the symptom in patients; and (iii) devise procedures which elicit the symptom in normal volunteers. In this way, we can achieve a truly experimental approach to the study of symptoms rather than relying on associations with cognitive impairments. As yet there is no cognitive account of symptoms in which the aims listed above have been fully achieved. The best

developed are probably the various attempts to explain auditory hallucinations and certain delusions in terms of defects in self-monitoring.

Hallucinations and self-monitoring

The basic proposal is that verbal hallucinations occur when the patient experiences his own speech or thought as coming from an external source. A straightforward prediction based on this idea is that hallucinating patients will have difficulty remembering whether a word they heard previously was spoken by themselves or by the experimenter. The results from studies using this approach have been equivocal^{2,21}. However, as yet, the appropriate paradigm for testing the hypothesis has not been used.

An elaboration of the self-monitoring theory considers how we know about our own actions. One theory is that we know that an action is our own because of feed-forward signals (corollary discharge) associated with the motor command¹⁹. These feed-forward signals enable us to modify behaviour and correct errors very rapidly since we do not have to wait for peripheral feedback about the effects of an action. Certain symptoms, including auditory hallucinations and delusions of control, might arise because the feed-forward signals associated with action are not properly monitored. In the absence of the feed-forward signal, patients would be dependent on peripheral feed-back for knowing about and modifying their own actions. A number of experiments have shown that, if peripheral visual feedback is eliminated, patients with passivity phenomena, such as delusions of control, have difficulty in making rapid error corrections and in remembering the actions they have just performed²²⁻²⁴. These results are consistent with a failure of the feed-forward mechanism. In an experiment specifically aimed at understanding auditory hallucinations, the patient's own speech was fed back in a distorted form²⁵. In these circumstances, many patients said that they could hear 'another voice saying the same things that I am saying'. Thus, distorting the peripheral feed back caused patients to attribute their own voice to an external source. In this case, we have effectively elicited a classic symptom by an experimental procedure derived from a cognitive model of symptom generation. False attributions were not made by normal controls or by patients who were currently symptom free or who had predominantly negative features. The false attributions were most likely to be made by patients concurrently experiencing both hallucinations and delusions.

The concept of corollary discharge was developed by physiologists, rather than psychologists²⁶ and so the self-monitoring model can readily be mapped onto brain function. In the case of vocalisation, there is evidence that signals arising in the anterior cingulate cortex (concerned with the initiation of vocalisation) are sent to auditory cortex causing modification of the response of this area to vocalisation²⁷. A recent brain imaging study has provided preliminary evidence (see chapter by Liddle) for functional disconnections between these areas in patients with schizophrenia²⁸.

Conclusions

While there is ample evidence that many patients with a diagnosis of schizophrenia perform badly on neuropsychological tests, it is not clear that there is a characteristic pattern of impairment associated with this diagnosis. Investigations of particular signs and symptoms are likely to be more fruitful, particularly if it is possible to develop models that explain these features in terms of underlying cognitive deficits. Some success has been achieved in explaining auditory hallucinations and certain passivity phenomena in terms of a defect in self-monitoring. Such a defect might be the result of functional disconnections between frontal areas concerned with initiating actions and posterior areas concerned with the perception of the effects of these actions.

Acknowledgements

I have benefited from several discussions about the neuropsychology of schizophrenia with Rhiannon Corcoran, Uta Frith and Karl Friston.

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