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Insight: its relationship with cognitive function, brain volume and symptoms in schizophrenia

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ABSTRACT

Background. Lack of insight is frequently observed in schizophrenia. Relationships have been noted between poor insight, clinical symptoms and cognitive impairments but the findings are inconsistent. There have been some recent attempts to relate poor insight to neuro-anatomical measures.

Method. We assessed insight, positive and negative symptoms of schizophrenia, cognitive performance, and whole brain volumes in a sample of 78 DSM-IV male schizophrenics and 36 normal male comparison subjects matched for age and IQ. Subjects underwent a dual-echo MRI brain scan to establish grey, white and whole brain volumes.

Results. Poor Wisconsin Card Sorting Test performance inversely correlated with insight in schizophrenic patients, as did the symptoms alogia, anhedonia, avolition/apathy, affective flattening, inappropriate affect, thought disorder and delusions. The presence of inappropriate affect, delusions and thought disorder, showed the most significant impact on insight levels. There were no significant correlations between whole brain, white and grey matter volume and degree of insight.

Conclusions. The results suggest that poor insight is significantly related to schizophrenic psychopathology, and confirm that there is a relationship between insight and executive performance. Awareness of illness is not related to any global brain measures, suggesting future investigations should pay attention to more specific cortical regions such as the frontal cortex.

INTRODUCTION

Insight is an elusive concept with a long history of divergent and inconsistent definitions and measurements (Amador & David, 1998). Lack of insight in psychosis can be conceived of as a multidimensional construct with a number of overlapping dimensions. These include the ability to recognize that one is ill, a capacity to re-label symptoms as pathological phenomena and compliance with treatment regimes (David, 1990). A number of theories exist concerning aetiology (David & Kemp, 1998). The two that have attracted the most empirical study are, first, that insight is an aspect of psychopathology, particularly delusions, and second that poor insight reflects a neuropsychological deficit (David & Kemp 1998).

Insight has been linked to both positive and negative symptoms in different patient groups (David *et al.* 1992; Amador *et al.* 1993, 1994; Kemp & Lambert, 1995; Collins *et al.* 1997; Smith *et al.* 2000; Goldberg *et al.* 2001; Buckley *et al.* 2001). Patients undergoing acute relapse (Sanz *et al.* 1998) as well as those with chronic conditions (Collins *et al.* 1997; Schwartz, 1998) show significant correlations between positive rather than negative symptoms and poor insight, whereas Cuesta & Zarzuela (1998) found a significant relationship in acute schizophrenics between poor insight and negative symptoms. Relationships have also been found between

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insight and a disorganised dimension (Amador *et al*. 1994; Lysaker & Bell, 1994; Kim *et al*. 1997; Cuesta & Zarzuela, 1998; Smith *et al*. 1998, 2000), grandiosity and overall severity (David *et al*. 1995; Kemp & Lambert, 1995; David & Kemp, 1998). Longitudinal studies have shown that psychotic symptoms are predictive of poor insight, at initial presentation (McEvoy *et al*. 1989), on recovery (Carroll *et al*. 1999), or both (Weiler *et al*. 2000) but not at 6-months follow-up (Fennig *et al*. 1996), while lack of insight is linked to recurrence and poorer outcome (David *et al*. 1995; Fennig *et al*. 1996; Schwartz *et al*. 1997), poorer global functioning (Pini *et al*. 2001) and poor treatment compliance (Smith *et al*. 1999; Donohoe *et al*. 2001).

The neuropsychological view of insight is that awareness of illness and relabelling of symptoms may be higher order cognitive abilities. Some authors have found that executive function tasks such as the Wisconsin Card Sorting Test administered to individuals with poor insight show increased preservative responses and/or poor concept formation (Young *et al*. 1993, 1998; Lysaker & Bell, 1994; Lysaker *et al*. 1998; Larøi *et al*. 2000). Individual components of insight have also been related to poor scores on executive function and fluency tests; a significant association was found between unawareness of symptoms and misattribution of negative symptoms and scores on such tests (Mohamed *et al*. 1999). Smith *et al*. (2000) reported that overall insight levels were not related to neuropsychological variables but more specifically, symptom misattribution, was correlated with card sorting performance. However, several studies have failed to demonstrate that poor insight is related to neuropsychological deficits, including card sorting (McEvoy *et al*. 1993; Cuesta & Peralta, 1994; Collins *et al*. 1997; Dickerson *et al*. 1997; Sanz *et al*. 1998; Goldberg *et al*. 2001; but see McEvoy *et al*. 1996). Many studies – nine out of 16 in a recent review (David, 1999) do show a relationship with general intelligence, which may be non-linear (David *et al*. 1995; Startup, 1996). One possible confound is duration of illness and the complexity of insight assessment used (Kemp *et al*. 1996).

In summary, the literature thus far suggests there may be a subgroup of schizophrenia patients with neuropsychological impairments that parallel those of insight, but there is a clearer relationship between insight and certain schizophrenic symptoms.

Few studies have looked at the relationship between insight and neuroanatomical measures. Takai *et al*. (1992) reported that using a single item on the Present State Examination (Wing *et al*. 1974) there was a significant correlation between lack of insight into illness and increased ventricle-brain ratios measured using MRI. David *et al*. (1995) were unable to show this in a larger sample using CT but the same insight measure. More recently, Flashman *et al*. (2000) showed that patients that are relatively unaware of their illnesses have smaller brain and intracranial volumes (brain tissue plus CSF) than either aware patients or healthy controls. However, they did not report any relationship, in their 30 schizophrenics, between levels of awareness and positive or negative symptoms, illness severity or educational level. In a secondary analysis, with 15 schizophrenic patients, they went on to show an inverse correlation between unawareness and bilateral middle frontal gyrus volume, and between symptom attribution and superior frontal gyrus volume (Flashman *et al*. 2001). Similarly, Larøi *et al*. (2000) reported that seven out of 13 patients had 'frontal lobe atrophy' on CT scans that correlated with poor insight.

This study was designed to assess insight and cognitive function in a large relatively homogeneous group of male schizophrenic patients, and establish which symptoms relate to insight, and whether a relationship exists between insight and whole brain measures. It was anticipated on the basis of published data, that the presence of positive symptoms especially hallucinations, delusions and thought disorder, would be associated with reduced levels of insight. It was also predicted, in agreement with some of the previous literature, that executive performance would show a significant correlation with the insight scores. Moreover, we sought to examine whether cerebral tissue volumes underpinned any relationship between cognitive function and insight. We predicted that there would be a significant relationship between grey matter volume and degree of insight (grey matter deficits being the most consistently found in schizophrenia, e.g. Wright *et al*. 1999) rather than the less specific increases in ventricular volume or ventricle–brain ratio.

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Table 1. *Demographic and clinical characteristics of patients and controls*

	Controls ($N=36$)		Schizophrenics ($N=78$)		Statistics	
	Mean	(S.D.)	Mean	(S.D.)		
Age	33·4	(8·93)	33·7	(8·50)	$F=0·03$	NS
No. years education	14·9	(3·36)	13·9	(2·30)	$F=4·05$	$P=0·05$
Handedness	29R, 7L		60R, 18L		$\chi^2=0·19$	NS
Age of onset	—		22·6	(5·32)	—	—
No. of months illness	—		134·3	(93·0)	—	—
Medication, CPZ equivalents*	—		648·2	(535·6)	—	—
Mean SAPS			1·23	(0·89)	—	—
Mean SAPS (minus Hallucination scores)	—		1·10	(0·85)	—	—
Mean SANS	—		1·79	(10)	—	—

CPZ, Chlorpromazine; SAPS, Scale for Assessment of Positive Symptoms; SANS, Scale for Assessment of Negative Symptoms; NS, non-significant; R, right; L, left.

* Patients on typical neuroleptics only.

METHOD

Subjects

Patients

A sample of 78 male schizophrenic patients was recruited from the in-patient and out-patient departments of the Maudsley Hospital, London. All were diagnosed as suffering from schizophrenia according to DSM-IV criteria (American Psychiatric Association, 1994) on the basis of clinical interview and chart review. Patients with a history of traumatic brain injury, epilepsy, alcohol or substance dependence or other neurological or psychiatric conditions were excluded. All subjects were between the ages of 18 and 55 years and had an estimated pre-morbid IQ as scored by the National Adult Reading Test (NART) (Nelson, 1982) of >90 (see Table 1). Current psychopathology was rated using the Scales for Assessment of Negative Symptoms (SANS) (Andreasen, 1984*a*) and the Scales for Assessment of Positive Symptoms (SAPS) (Andreasen, 1984*b*) to neuropsychological testing. The SANS measures each of five negative symptom complexes: alogia, affective flattening, avolition–apathy, anhedonia–asociality, and attentional impairment while the SAPS measures the positive symptom complexes of hallucinations, delusions, bizarre behaviour, positive formal thought disorder and inappropriate affect. For analysis we used the global scores for each of the five negative symptom complexes and the four global scores for the positive symptom complexes. The final symptom category on the SAPS is inappropriate affect; this is a single item rather than a global score. However, for ease of terminology we later refer to the 'global' scores for each of the 10 symptom complexes.

Normal controls

Thirty-six normal male controls were also recruited for the study by advertisement in two local London job centres.

MRI measures

Seventy-one schizophrenic and 31 normal control subjects had MRI scans of their brain. Seven schizophrenics and five controls either refused to be scanned or became claustrophobic and were unable to complete the procedure. Images were obtained using a 1.5 Tesla General Electric Signa MR system (GE, Milwaukee, WI, USA). Dual echo fast spin echo images were acquired (repetition time (TR) = 4000 ms, effective echo times (TE_1) = 20 ms (TE_2) = 100 ms) with an echo train of 8. This was a near-coronal sequence angled parallel to the clivus, with 60 contiguous 3 mm thick slices with an in plane field of view of 22 cm and a 256×256 acquisition matrix. Image contrast for all datasets was chosen using a software tool for optimizing image contrast (Simmons *et al.* 1996). These images were used to calculate whole brain volume as well as grey, and white matter and total CSF volumes (see Bullmore *et al.* 1995; Suckling *et al.* 1999; Shapleske *et al.* 2001 for detailed description of the method).

Cognitive assessment

Insight was measured using the expanded Schedule of Assessment of Insight (SAI-E)

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(Kemp & David, 1997; Sanz *et al*. 1998). This is a semi-structured interview that records three separate dimensions of insight; treatment compliance (0–4); recognition of illness (0–6); and relabelling of psychotic phenomena, and also included one supplementary question on hypothetical contradiction (0–4). The expanded version includes items on awareness of change in mental functioning, awareness of need for treatment and awareness of the psychosocial consequences of the illness.

General cognitive measures

A short version of the Wechsler Adult Intelligence Scale Revised (WAIS-R) (Wechsler, 1981) was used as a measure of general cognitive functioning. The tests included: Information, Digit Span, Digit Symbol and Block Design. A predictive current IQ score was calculated from these four measures. Also used was the Visual Span from the Wechsler Memory Scale-R, to test visual working memory.

Executive function

A small battery of neuropsychological tests were also administered, these included the Wisconsin Card Sort Test (WCST) (Heaton, 1981), a classical 'frontal lobe' task highlighting maintenance of set and cognitive flexibility. Two of the most clinically relevant scores are categories achieved (CA) and preservative responses (PR).

To assess attention and sustained concentration aspects of executive function the Continuous Performance Task (CPT) (Nuechterlein *et al*. 1992) AX version was included. In this subjects are required to press a response key each time they see the letter X preceded by the letter A. The total duration of the task was 10 min. There were 50 AX combinations, 50 combinations of X preceded by a letter other than A and 50 combinations of A not followed by the letter X. The rest of the stimuli were fillers. We rated subjects on five performance measures: mean reaction time (RT) for a correct response, number of correct responses, number of false alarms, number of missed responses.

The Controlled Oral Word Association Test (Benton, 1976) was used to assess phonological fluency or verbal flexibility. Using the letters F, A and S, subjects are required to produce verbally as many words as possible that begin with the target letter, excluding proper nouns and places (1 min for each letter).

Statistics

Correlations using Pearson product moment were used to investigate the relationship between levels of insight and the following variables: (*a*) demographics; (*b*) cognitive performance; (*c*) clinical symptoms; and (*d*) brain volumes. We predicted that positive symptoms, tests of executive function and grey matter would all show significant correlations. We also used correlational analysis to investigate the relationship between NART IQ and the other cognitive measures. Subsequently, we entered any significant variables outlined in the correlational analysis above into a multiple regression analysis to examine which variables had the most significant impact on levels of insight.

RESULTS

There was no significant difference in age, or IQ as scored by the NART (Nelson, 1982) or handedness (Edinburgh Inventory) (Oldfield, 1971) between the controls and patients (Table 1). The patient group showed similar scores across each of the questions in the insight assessment; questions 1–8, mean ($\pm$S.D.) scores ranged from 1·28 (0·7) to 1·74 (0·5) and questions 9–11 from 2·0 (1·2) to 2·85 (1·38).

Demographics

We used total insight score to correlate with the following demographic variables: age, number of years in education, age of onset, number of months ill and daily medication dose in CPZ equivalents. There was only one significant positive correlation: between insight and number of years in education ($r = 0{\cdot}3$ $P < 0{\cdot}05$). Number of years in education is often used as a proxy IQ measure.

Cognitive performance

Table 2 shows the mean scores for each of the tasks used in the cognitive assessment for each of the two subject groups. Oneway ANOVA demonstrated that there were no significant group differences on the NART (as predicted as this was a matching variable), also WCST PR, CPT mean RT for a correct response, CPT total number of correct responses, false alarms and

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Table 2. *Cognitive assessment of patients and controls*

Task	Score	Controls ($N=36$) Mean	(S.D.)	Schizophrenics ($N=78$) Mean	(S.D.)	F	P
(NART) IQ		115·7	(8·6)	112·8	(10·2)	2·2	NS
WAIS-R		110·5	(13·5)	95·8	(15·9)	23·0	0·001
WMS-R	Visual Span	19·0	(5·8)	18·0	(5·3)	0·54	NS
WCST	CA	4·5	(2·1)	3·5	(2·0)	6·5	0·05
	PR	28·2	(20·7)	34·7	(21·3)	2·3	NS
CPT	Mean RT	352·8	(79·8)	378·1	(90·6)	2·1	NS
	Correct	46·7	(10·2)	45·5	(9·4)	0·41	NS
	False alarms	5·3	(132·0)	12·2	(23·7)	2·7	NS
	Miss	3·2	(10·2)	4·8	(10·0)	0·61	NS
Verbal Fluency (FAS)*	Total score	47·7	(13·1)	35·4	(14·3)	17·0	0·001

(NART) IQ, National Adult Reading Test; WAIS-R, Weschler Adult Intelligence Scale Revised; WMS-R, Weschler Memory Scale Revised; WCST, Wisconsin Card Sorting Tests; CA, categories achieved; PR, perseverative responses; CPT, Continuous Performance Test; NS, non-significant.

* FAS, fluency for words beginning with letters F, A and S.

misses. There were however, group differences on all other cognitive variables, such as current IQ score from the WAIS-R and the total score on the verbal fluency test ($P<0·001$). The number of categories achieved on the WCST was also significantly different between the two subject groups ($P<0·05$).

We further examined whether NART IQ correlated with any of the other cognitive measures in both subject groups. In the patient group Pearson's product moment correlations between NART IQ and other cognitive measures revealed there were significant correlations with current WAIS IQ ($r=0·62$, $P<0·001$), categories achieved ($r=0·33$, $P<0·006$), perseverative responses ($r=-0·26$, $P<0·05$), verbal fluency ($r=0·42$, $P<0·001$) and visual span ($r=0·46$, $P<0·001$). In controls, NART IQ correlated with current WAIS IQ ($r=0·68$, $P<0·001$), verbal fluency ($r=0·65$, $P<0·001$) and visual span ($r=0·49$, $P<0·009$).

Fig. 1(*a*) shows significant Pearson's product moment correlations between the total insight score and each of the cognitive variables in the schizophrenia patient group. NART IQ and WCST categories achieved were positively correlated with insight ($P<0·05$), and current WAIS-R IQ showed a trend towards a significant relationship with insight ($P=0·06$), i.e. better performance on each of the measures was associated with a higher insight score. The only WAIS-R subscale to correlate significantly with insight was Information. None of the other tests correlated significantly.

Clinical symptoms

Fig. 1(*b*) shows significant Pearson's product moment correlations between the total insight score and the 10 SANS and SAPS global scores outlined above, in the schizophrenia group. They showed significant correlations for the following negative symptoms from the SANS – global alogia, global anhedonia, global avolition/apathy and global affective flattening; and the following positive symptoms from the SAPS – global formal thought disorder, global delusions and inappropriate affect. In all cases a higher insight score was associated with less severe symptoms.

Brain volumes

Table 3 shows the mean grey, white, CSF and total brain matter volumes for both the schizophrenic and the control groups. Schizophrenics had significantly smaller white matter and total brain volumes than the control subjects. There were no significant correlations between total insight score and grey, white, CSF and total brain matter volumes, in the schizophrenic group, (all $r<0·1$) (grey $P=0·54$, white $P=0·74$, CSF $P=0·65$ and total $P=0·58$).

Regression analysis

To confirm which factors had the most impact on insight performance the following multiple regression analysis was performed. Nine variables were identified in the correlational analysis as having a significant relationship with insight.

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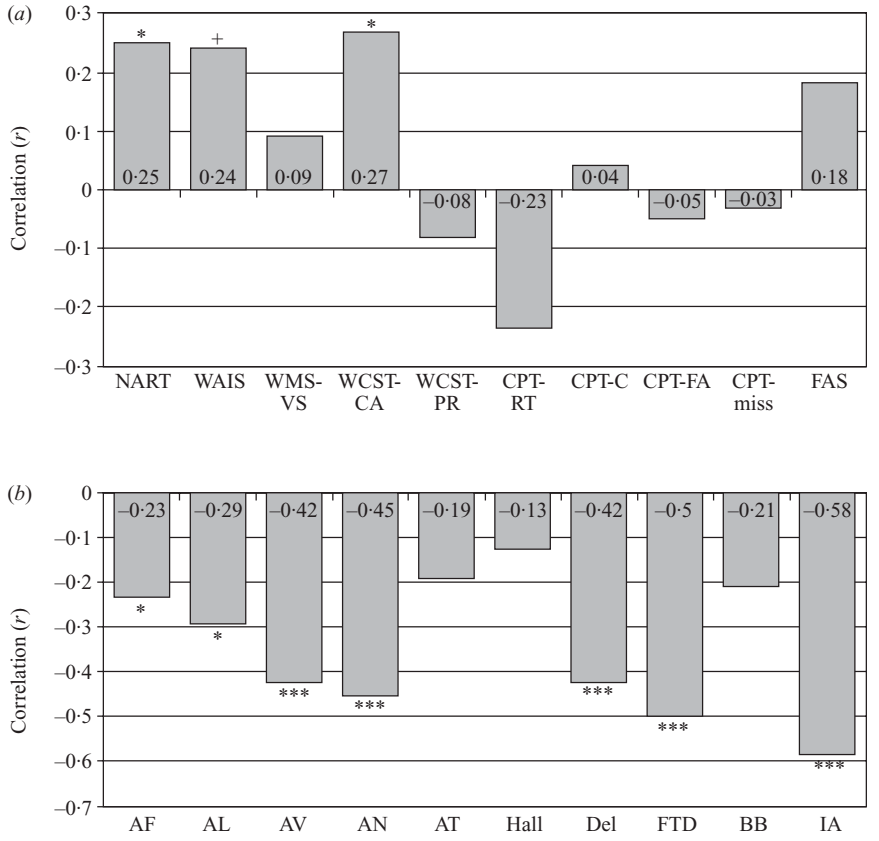


FIG. 1. (*a*) Correlations of total insight score with cognitive measures. (NART, National Adult Reading Task; WAIS, Weschler Adult Intelligence Scale; WMS-VS, Weschler Memory Scale visual span; WCST-CA, Wisconsin Card Sorting Test categories achieved, WCST-PR, perseverative responses; CPT-RT, Continuous Performance Task reaction time; CPT-C, number correct; CPT-FA, false alarms; CPT-miss, number of misses; FAS, verbal fluency score. $^{+}P=0{\cdot}06$; $^{*}P<0{\cdot}05$.)
(*b*) Correlations of total insight score with clinical measures. (AF, Affective flattening; AL, alogia; AV, avolition and apathy; AN, anhedonia; AT, attention; Hall, hallucinations; Del, delusions; FTD, formal thought disorder; BB, bizarre behaviour; IA, inappropriate affect. $^{*}P<0{\cdot}05$; $^{***}P<0{\cdot}001$.)

These were seven 'global' symptom ratings from the SANS/SAPS (affective flattening, alogia, avolition, anhedonia, delusions, thought disorder and affective flattening), and two cognitive variables (NART IQ and WCST CA). As brain volumes did not show a significant correlation with insight none of these variables were used. The significant variables were entered into a stepwise regression of the total insight score. This analysis established that three key symptoms accounted for the greatest variation in insight score. These symptoms were inappropriate affect, delusions and formal thought disorder, they accounted for 50·5% of variation ($F(3, 72)=21{\cdot}7$ $P<0{\cdot}001$). The two cognitive factors were not significant in the model.

DISCUSSION

The results of this study confirmed that insight was related to a number of different positive and negative symptoms, as well as showing that a relationship did exist between insight and some measures of cognitive function including certain executive abilities.

Thought disorder and delusions were the most prominent positive symptoms, plus inappropriate affect (which may be classified as a facet of disorganization) which, when present, were associated with poor insight (see Amador *et al.* 1994; Lysaker & Bell, 1994; Collins *et al.* 1997; Kim *et al.* 1997; Cuesta & Zarzuelta, 1998; Smith *et al.* 1998; Carroll *et al.* 1999; Buckley *et al.*

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Table 3. *MRI brain volumes in patients and controls*

	Controls ($N=31$)		Schizophrenics ($N=71$)			
Brain volume	Mean	(S.D.)	Mean	(S.D.)	F	P
Grey matter	585·8	(67·1)	571·4	(71·1)	0·91	0·34
White matter	544·0	(77·0)	507·5	(71·7)	5·4	0·02
Cerebro-spinal fluid	167·7	(53·7)	159·0	(50·4)	0·60	0·43
Total brain volume	1300·8	(96·7)	1235·7	(108·9)	8·2	0·005

2001; Goldberg *et al.* 2001). Thought disorder and delusions could both be characterized as loosening of 'normal' everyday associations and difficulties with reasoning, thus it may not be surprising that when these symptoms are present patients have deficient awareness of their illness. Regarding delusions, the strength with which one holds a belief, and maintaining it as possibly untrue, may be considered as two sides of the same coin. There was only a weak relationship between poor insight and the presence of hallucinations, suggesting that patients with hallucinations are more aware that this symptom is a deviation from the norm or find it relatively easy to relabel them as, for example 'the voices' (see also Nayani & David, 1996). Additionally, there were a number of negative symptoms that showed a significant correlation with poor insight, i.e. anhedonia, alogia, avolition and affective flattening, although these variables were not major predictors of insight levels in the regression analysis. This is in line with previous studies that demonstrate that negative symptoms show a rather weaker association with insight than positive symptoms (Collins *et al.* 1997; Carroll *et al.* 1999).

The results also confirmed the more equivocal finding reported in the literature of a relationship between neuropsychological performance and degree of insight (i.e. Young *et al.* 1993, 1998; McEvoy *et al.* 1996; Lysaker *et al.* 1998; Smith *et al.* 2000). This association was limited to verbal IQ measures and number of categories achieved on the WCST, but not perseverative responses and was to a significant extent confounded by the presence of psychotic symptoms. Furthermore, the fluency tests and CPT performance (both false alarms and misses) were not correlated with insight. These results mirror those of Young *et al.* (1993) and Lysaker *et al.* (1998). Mohammed *et al.* (1999) also found that the categories achieved variable was associated with unawareness of positive symptoms rather than perseverations. Hence, if there is a connection between executive function and insight it is likely to be rather specific. Working memory, initiation, and retrieval of stored semantic information do not seem to be relevant while aspects of concept formation and also shift behaviour may be.

It is noteworthy that comparisons between patients with schizophrenia and controls on the WCST show larger effect sizes for the number of categories achieved than preservative errors, although intelligence is an important confounder (Laws, 1999). Verbal intelligence and estimates of pre-morbid IQ (including years of education) correlated with insight scores, a consistent finding in the research literature (reviewed in David, 1999). However, it is possible that this correlation could be a result of possessing the vocabulary sufficient to convey the presence of insight to the satisfaction of the clinician. Semi-structured and reliable methods of assessing insight counteract this problem to some extent, as does the use of relatively language-free tests such as card sorting.

Despite significant group differences in total brain volume, with schizophrenics having smaller overall brain volumes, the results of this study did not confirm a relationship between grey matter volume and insight performance, nor was there a relationship to total brain volume, white matter or CSF. These results are in direct contrast to Flashman *et al.* (2000), who reported such findings using 30 patients with schizophrenia. Therefore, we contend that there is not a robust relationship between total brain volume and insight using a larger, and thus, more reliable, group of subjects. It may be the case that more specific regions of the brain can be related to insight performance, for example, specific frontal lobe abnormalities (Larøi *et al.* 2000; Flashman *et al.* 2001). More directed study of this kind might reveal significant relationships.

It is generally accepted that executive abilities are related to prefrontal cortex function (e.g. Duncan & Owen, 2000; Funahashi, 2001). Further study should examine the relationship between level of insight and volume of the prefrontal cortex using more detailed MRI measures, while controlling for symptom scores. The frontal lobes are not homogeneous in

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function and different sub-regions may correlate with awareness, as shown in Flashman *et al*. (2001). Similarly, modern insight research (David *et al*. 1992; Amador *et al*. 1993) conceptualizes insight as having more than one component or dimension. Future research needs to utilize these dimensions and examine whether, individually they relate to symptoms, cognitive deficits or neuro-anatomical measures. We would predict that the ability to re-label or attribute symptoms to a medical condition would be particularly dependent on executive skills and dorsolateral or medial pre-frontal regions rather than, say, treatment compliance, which is more influenced by social factors.

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