Dyspraxia and agnosia in schizophrenia

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A battery of tests for dyspraxia and agnosia was administered to 51 chronic schizophrenic patients to test the hypothesis that these cortical neurological signs are associated with psychomotor poverty syndrome (poverty of speech, flat affect, decreased spontaneous movement), disorganization syndrome (various disorders of the form of thought, inappropriate affect), abnormal involuntary movements, cognitive impairment, and duration of illness. The findings supported all elements of the hypothesis, and in particular, demonstrated a strong correlation of cortical signs with psychomotor poverty and with cognitive impairment.

Keywords: Association cortex – Disorganization – Negative symptoms – Neurological signs – Psychomotor poverty – Reality distortion – Schizophrenia

INTRODUCTION

The functions of the association areas of the cerebral cortex include the processing of sensory information (gnosis) and the coordination of motor activity (praxis). Following Luria (1980), we shall designate abnormalities of these higher cortical functions as cortical neurological signs. Some schizophrenic patients suffer impairment of motor coordination and processing of sensory information (Rochford *et al.*, 1970; Quitkin *et al.*, 1976; Manschreck *et al.*, 1982; Liddle, 1987a). In this paper we examine the relationship between these cortical neurological signs and various other phenomena occurring in schizophrenia, such as psychotic symptoms, cognitive impairment, abnormal involuntary movements and parkinsonism.

Crow (1980) proposed that there are two independent dimensions of psychopathology in schizophrenia. Type 1, which tends to be predominant in acute episodes of illness, is characterized by positive symptoms such as delusions, hallucinations and formal thought disorder. Type 2, which tends to be chronic, is characterized by negative symptoms such as poverty of speech and flatness of affect. Crow proposed that type 2 is associated with structural disorder of the brain. Evidence from X-ray computed tomography (CT) studies provides some support for this proposal. In a review of CT in schizophrenia, Lewis (1990) reported that five of the 18 studies which have addressed the issue found a significant association between negative symptoms and ventricular enlargement. Crow also proposed that type 2 schizophrenia would be associated with neuro-

logical abnormalities, especially those characteristic of subcortical disorder such as abnormal involuntary movements (Crow *et al.*, 1983). This proposal is consistent with the evidence suggesting that some aspect of the psychopathology of schizophrenia predisposes to both abnormal involuntary movement and to negative symptoms (Liddle *et al.*, 1993), but this issue remains controversial.

Thus, despite remaining uncertainties, there is evidence to support the hypothesis implicit in Crow's concept of type 2 schizophrenia, that negative symptoms, abnormal involuntary movements and chronicity are associated with diffuse brain abnormalities involving both cortical and subcortical neurons. If this is so, it would be predicted that cortical neurological signs would be associated with negative symptoms, with chronicity, with cognitive impairment and with neurological signs characteristic of basal ganglia disorder.

While the type 1/type 2 distinction has provided a valuable foundation for exploration of the heterogeneity of schizophrenia, it does not account adequately for the observed clinical correlates of formal thought disorder. In his original formulation Crow (1980) classified formal thought disorder as a positive symptom belonging to the type 1 syndrome. While this is consistent with the occurrence of florid formal thought disorder during acute episodes of illness, there is a substantial body of evidence (reviewed by Barnes and Liddle, 1990) suggesting that

formal thought disorder has some of the characteristics attributed to symptoms of the type 2 syndrome. In particular, formal thought disorder is associated with cognitive impairment (Allen, 1983; Liddle 1987a) and with poor occupational adjustment (Harrow *et al.*, 1983; Liddle, 1987b).

A possible resolution to the question of whether formal thought disorder should be regarded as a type 1 or a type 2 symptom is provided by studies which have used factor analysis to examine the patterns of correlations between schizophrenic symptoms. Liddle (1984, 1987b) found that schizophrenic symptoms segregate into three syndromes: psychomotor poverty (poverty of speech, flat affect, decreased spontaneous movement), disorganization (various disorders of the form of thought, inappropriate affect) and reality distortion (various delusions and hallucinations). Similar findings of a segregation of schizophrenic symptoms into three syndromes have been reported by many others including Bilder *et al.* (1985), Arndt *et al.* (1991) and Frith (1992). Liddle (1987a) found that each of the three syndromes was associated with a distinguishable pattern of neuropsychological impairment, suggesting that there are at least three distinguishable though related pathological processes underlying the symptoms of schizophrenia. This hypothesis was confirmed by a study using positron emission tomography in which it was found that each of the three syndromes was associated with a specific pattern of regional cerebral blood flow. Furthermore, Liddle (1987a) found that both the psychomotor poverty syndrome and the disorganization syndrome were associated with cortical neurological signs.

Manschreck *et al.* (1982) examined the relationship between disturbed voluntary motor activity and schizophrenic symptoms, and found that disordered motor activity was associated with formal thought disorder. This is consistent with the hypothesis that there is a pathological process in schizophrenia that leads to the disorganization of thinking, affect and motor activity.

On the basis of the evidence supporting the hypothesis that type 2 schizophrenia is associated with diffuse cortical and subcortical abnormality, together with Liddle's finding that the psychomotor poverty and disorganization syndromes are both associated with cortical neurological signs, and Manschreck's evidence that defects of motor synchrony are associated with formal thought disorder, we set out to test the hypothesis that cortical signs in schizophrenia are associated with: (1) psychomotor poverty syndrome; (2) disorganization syndrome; (3) chronicity; (4) cognitive impairment; and (5) abnormal involuntary movements.

This study was carried out with the approval of the Research Ethics Committee of Riverside Health Authority.

METHOD

Subjects

All 57 patients resident in three long-stay and two rehabilitation wards at Horton Hospital, satisfying DSM-III criteria for schizophrenia (American Psychiatric Association, 1980) and aged less than 66 years, were approached, and 51 gave informed consent to participate in the study. Their mean age was 51.3 years (range 31-65), and mean duration of illness was 27.8 years (range 9-43). There were 33 males and 18 females. Forty-nine were receiving antipsychotic medication (though none were receiving atypical antipsychotics), and for these 49 patients the mean daily dose in chlorpromazine equivalents was 1282 mg (range 72-7457).

Symptom assessment

Symptoms were assessed (by P.F.L.) according to the Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1982) and the Manchester scale (Krawieka *et al.*, 1977). The Manchester scale includes a concise rating of delusions, hallucinations and formal thought disorder, and is especially suitable for use with severely disabled patients who cannot maintain concentration in a long interview. Liddle (1987b) had originally used Andreasen's SANS and SAPS (Scale for the Assessment of Positive Symptoms) in the delineation of the three syndromes, but Liddle and Barnes (1990) have subsequently demonstrated that the three syndromes can be identified using SANS ratings of negative symptoms and Manchester scale ratings for delusions, hallucinations and formal thought disorder. Syndrome scores were assigned according to the procedure used originally by Liddle (1987a), with the modification that the SAPS global scores for delusions, hallucinations and positive formal thought disorder were replaced by the corresponding Manchester scale items.

Neurological assessment

Cortical signs were assessed (by S.H.) according to a rating scale based on that used previously by Liddle (1987a) with added motor coordination tests developed by Luria (1980). There were 10 motor items: finger-thumb opposition (right and left sided); forearm pronation-supination (right and left); forming a fist alternating with opposition of finger and thumb to create a ring (right and left); sequential presentation of fist, edge of hand and palm (right and left); alternately clenching and opening fist while performing the opposite movement with the other hand. There were six sensory items: graphaesthesia (right and left); stereognosis (right and left); and tactile inattention during bilateral stimulation (inattention on right and left rated separately). Verbal articulation was also assessed. Each item was rated 0 (no impairment), 1 (mild

impairment), 2 (moderate) or 3 (severe). A glossary defining each item, and specifying guidelines for rating is available from P.F.L. A total cortical sign score can be obtained by adding the item scores. A score for dyspraxia can be derived by summing the motor coordination items, and a score for agnosia derived by summing the items concerned with sensory processing. In addition, most of the items involve separate assessment of the right and left side of the body and separate scores for right- and left-sided signs can be derived by summing scores for each side of the body separately.

Abnormal involuntary movements were assessed (by T.R.E.B.) according to the procedure described by Barnes and Trauer (1982). Parkinsonism was assessed (by T.R.E.B.) using the scale of Simpson and Angus (1970). Akathisia was assessed (by T.R.E.B.) using the Barnes scale for akathisia (Barnes, 1989).

Cognitive assessment

A brief battery of memory tests from the Wechsler Memory Scale (Wechsler, 1945) including immediate and delayed logical memory, immediate and delayed memory for designs tests, and digit span, together with the Corsi blocks test which is a spatial analogue of digit span, was administered (by P.F.L.). In addition, D.L.M. administered a battery of frontal lobe tests, including FAS verbal fluency test (Borkowski *et al.*, 1967); the Stroop RCN₁ and Stroop NCW₁ tests (Stroop, 1935); the modified card sorting test (Nelson, 1976); and trails A and B from the Halstead-Reitan battery (Reitan, 1958), together with the graded naming test (McKenna and Warrington, 1983) which provides an approximate measure of general intelligence, to the 43 patients from four of the five wards. Not all of the patients were able to complete all of the frontal lobe tests. Of the seven separate tests in this battery, the mean number of tests completed per patient was 6.1. The relationship between frontal test performance and symptoms in this subgroup of patients is reported in a separate paper (Liddle and Morris, 1991). While there was a significant negative association between number of tests completed and global severity of symptoms (measured by adding scores for all nine Manchester scale items), there were no statistically significant relationships between

scores for the individual syndromes and the number of tests completed.

Data analysis

Pearson correlations of total cortical sign scores (and where relevant, the various cortical sign subscores) with syndrome scores, global symptom severity, illness duration, abnormal involuntary movement scores and cognitive test scores were calculated. Two-tailed tests of significance were employed, though less conservative one-tailed tests might have been permissible for the majority of tests in which specific hypotheses were being tested. Partial correlations were calculated to allow for variation in potentially confounding variables such as age.

RESULTS

In this group of patients there was a high prevalence of cortical signs. The mean value of the total cortical sign score per patient was 19.9 (S.D. 9.4, range 5-44). The maximum possible total score is 48. For all except one of the 51 patients, a rating of moderate or severe impairment was made for at least one cortical sign. Forty-five patients had a rating of moderate or severe impairment for at least one of the nine dyspraxia items, while 40 patients had a rating of moderate or severe impairment for at least one of the six agnosia items. There was no significant difference between the scores for right-sided signs (mean 8.9, S.D. 4.4) and the score for left-sided signs (mean 8.6, S.D. 4.4).

Relationship to syndromes

The relationships between syndrome scores and cortical signs are shown in Table I. It can be seen that psychomotor poverty was associated with dyspraxia, agnosia, left-sided, right-sided and total cortical signs scores. There was a trend towards stronger association with apraxia than with agnosia. Disorganization was associated less strongly with cortical signs, though the correlations with total score and subscale scores for agnosia, for left-sided and for right-sided signs were none the less significant at the level $p < 0.05$. In contrast to the situation with psychomotor poverty, the strongest correlation was with agnosia. The reality distortion syndrome was not associated with any of the cortical sign scores.

TABLE I. Correlations between syndrome scores and cortical signs

	Psychomotor poverty	Disorganization	Reality distortion
Dyspraxia	0.55***	0.27	0.04
Agnosia	0.35*	0.33*	-0.02
Right-sided signs	0.47**	0.31*	0.10
Left-sided signs	0.45**	0.29*	-0.02
Cortical sign total	0.46**	0.28*	0.06

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$, two-tailed.

The pattern of partial correlations between cortical sign scores and syndromes allowing for variation in age was very similar to the pattern of first-order correlation coefficients. All of the statistically significant relationships shown in Table I remained significant after allowing for variation in age.

Relationship to signs characteristic of basal ganglion disorder

There was a moderate, but the none the less significant correlation between cortical sign total and orofacial dyskinesia ($r = 0.30$, $p < 0.05$). However, the correlation between cortical sign total and trunk-and-limb dyskinesia was small and statistically insignificant ($r = 0.16$), indicating that it is unlikely that the association between cortical signs and involuntary movements was due merely to interference by involuntary trunk and limb movements with the coordination of motor activity.

Cortical sign total was also significantly related to parkinsonism ($r = 0.40$, $p < 0.01$). While the correlation with dyspraxia was strong ($r = 0.52$, $p < 0.001$), that with agnosia was weak ($r = 0.11$), making it difficult to exclude the possibility that the observed association between cortical signs and parkinsonism merely reflects the interference of tremor or rigidity with the coordination of motor activity, rather than an intrinsic relationship between parkinsonism and cortical malfunction. The correlation between akathisia and cortical sign total was small ($r = 0.14$) and not statistically significant.

Relationship to cognitive impairment

The relationship between cortical signs and cognitive impairment is shown in Table II. Cortical sign total is

significantly correlated with impairment in virtually all aspects of cognitive function assessed. The strongest correlation is with impaired performance in the graded naming test.

There were only two tests for which there was not a significant correlation with cortical signs; digit span and the modified card sorting test. In the case of digit span, the absence of correlation probably reflects the fact that this was the only test in which the patients' performance was not substantially impaired. The mean digit span for the group was 5.7 (S.D. 1.3). The expected digit span for a normal population of similar age is 6. However, in the case of percentage perseverative errors in the modified card sorting test, 17 of the 41 patients completing this test exhibited a percentage perseverative error score greater than 50% which is the criterion for frontal lobe impairment (Nelson, 1976).

Relationship to duration of illness, age and medication

Total cortical sign score was correlated with duration of illness ($r = 0.41$, $p < 0.01$) and with age ($r = 0.43$, $p < 0.01$), but not with age at onset of illness ($r = 0.03$). The partial correlation between cortical sign score and duration of illness allowing for variation in age was only 0.13, suggesting that the relationship between cortical signs and duration of illness is related to age. The correlation between current dose of antipsychotic medication (measured in chlorpromazine equivalents) and cortical sign total was insignificant ($r = -0.13$).

DISCUSSION

The hypothesis that cortical signs would be associated with the psychomotor poverty syndrome was confirmed. This association applied to dyspraxia and agnosia, and to left- and right-sided cortical signs. There was a trend towards a stronger correlation of psychomotor poverty with dyspraxia than with agnosia, consistent with the finding by Liddle *et al.* (1992) that the psychomotor poverty syndrome is associated with decreased blood flow in an extensive region of prefrontal cortex, and in a circumscribed area of left parietal cortex. Since the symptoms of the psychomotor poverty syndrome are the core negative symptoms which Crow proposed were characteristic of the type 2 syndrome, this study suggests that cortical signs should be considered a component of the type 2 syndrome.

The hypothesis that cortical signs would be associated with the disorganization syndrome received moderate support. The finding that disorganization was associated with agnosia is consistent with the finding by Liddle *et al.* (1992) that the disorganization syndrome is associated with decreased blood flow in parietal cortex bilaterally, in addition to association with decreased flow in the ventral

TABLE II. Correlations between cortical sign total score and neuropsychological test scores

	Cortical sign total
Logical memory†	-0.46**
Delayed logical memory†	-0.44**
Memory for designs†	-0.63***
Delayed memory for designs†	-0.62***
Digit span†	-0.25
Corsi blocks†	-0.51***
Graded naming test†	-0.66***
Stroop RCN ₆	0.48**
Stroop NCW ₆	0.60***
Verbal fluency†	-0.46**
Halstead-Reitan trails A	0.44**
Halstead-Reitan trails B	0.39*
Modified card sorting test	
Number of categories achieved	-0.36*
Total errors	0.38*
Percent perseverative errors	0.01

For those tests marked † higher score denotes better performance; for all other tests, higher score denotes greater impairment.

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$, two-tailed.

prefrontal cortex and with increased flow in the anterior cingulate. The hypothesis that cortical signs would be associated with abnormal involuntary movements was confirmed, though the correlation was of moderate magnitude and applied only to orofacial movements. The fact that there was no evidence of substantial correlation of cortical signs with trunk and limb movements makes it unlikely that the association with involuntary movements was due to interference with motor coordination at a peripheral level, and suggests an intrinsic relationship between cortical and subcortical malfunction. This might indicate that the underlying neuronal disorder involves both cortical and subcortical neurons. Alternatively, the reciprocal connections between cortical and subcortical structures make it possible that disorders of cortical function might arise from subcortical damage. It is therefore necessary to be cautious in interpreting cortical signs as evidence of direct damage to cortical neurons.

The hypothesis that cortical signs would be associated with cognitive impairment was strongly confirmed. There was a significant association with impairment in a wide variety of aspects of cognitive function, including object naming, memory, and various tasks assessing the initiation and flexibility of mental processing, tasks which are often impaired in patients with frontal lobe damage. However, one specific index of frontal lobe damage, namely the tendency to produce perseverative errors in the card sorting test, was not associated with cortical sign score, despite the fact that a substantial number of the patients fulfilled the criterion indicating frontal lobe impairment in this test. Liddle and Morris (1991) found that perseverative errors on card sorting was strongly associated with the disorganization syndrome, but not with the psychomotor poverty syndrome. Thus it appears that a tendency to produce perseverative errors is related to a specific aspect of the psychopathology of schizophrenia which is not significantly related to cortical signs.

The hypothesis that cortical signs would be associated with duration of illness was supported, though it is possible that the major part of this association could be accounted for by the effects of age. It is necessary to be cautious in assuming causal relationships. While it is possible that age-related neuronal degeneration might contribute to the development of cortical signs, it is also possible that cortical signs and associated cognitive impairment might militate against discharge from hospital, leaving a high proportion of cases with cortical signs among the older patients.

This study provides at least a moderate level of support for all elements of the hypothesis tested, and in particular, provides strong evidence for an association of cortical signs with the psychomotor poverty syndrome and with cognitive impairment. There are two possible interpretations of these findings. One possibility is that cortical

signs might be a non-specific index of brain damage which predisposes to the development of schizophrenia with marked psychomotor poverty symptoms, and to a lesser extent, disorganization symptoms. The other possibility is that cortical signs are an expression of the specific pathological processes underlying the psychomotor poverty syndrome and the disorganization syndrome. Insofar as psychomotor poverty and disorganization showed a somewhat similar pattern of association with the different cortical sign subscale scores, the evidence suggests that cortical signs are a relatively non-specific index of brain damage in schizophrenia. None the less, there was a trend for psychomotor poverty to be associated more strongly with dyspraxia than with agnosia, and for disorganization to be associated more strongly with agnosia than with dyspraxia. This difference is consistent with the difference in patterns of cerebral blood flow associated with each of the two syndromes (Liddle *et al.*, 1992). Thus there is some evidence for a degree of specificity in the relationships between cortical signs and schizophrenic syndromes.

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