SPET study of verbal fluency in schizophrenia and epilepsy

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Background The association between temporal lobe epilepsy and schizophrenia suggests that the critical abnormality may be pathology within the temporal lobes. People with schizophrenia-like psychosis of epilepsy (SLPE) provide a useful group in which to examine the importance of temporal and frontal lobe dysfunction in schizophrenia.

Method A verbal fluency activation paradigm and a ^{99m}Tc HMPAO SPET were used to study frontotemporal function in people with SLPE (n=12), schizophrenia (n=11) and epilepsy (n=16).

Results People with SLPE differed from both other groups by showing lower blood flow in the left superior temporal gyrus during performance of a verbal fluency task compared with a word repetition task (F=5.4, P=0.01). During the verbal fluency task people with primary schizophrenia showed a greater increase in blood flow in anterior cingulate (F=4.5, P=0.02) than the other two groups. There were no between-group differences in frontal brain regions.

Conclusion Our findings support an association between left temporal lobe abnormality and SLPE. The different patterns of activation observed in people with primary schizophrenia and SLPE suggests that different pathophysiological mechanisms may operate in these two groups. In SLPE the pathophysiology may be relatively confined to the dominant temporal lobe.

People with epilepsy are at increased risk of developing an illness which closely resembles schizophrenia, known as schizophrenia-like psychosis of epilepsy (SLPE). This risk is thought to be greatest for people with temporal lobe seizures arising in the left hemisphere (Flor-Henry, 1969). Left temporal lobe abnormalities have been described in primary schizophrenia, but other brain regions have been implicated. In particular, prefrontal abnormalities have been reported and frontotemporal dysfunction has been proposed as an important pathophysiological mechanism (Weinberger *et al*, 1992). SLPE may be a 'mock-up' of primary schizophrenia, in which case prefrontal abnormalities should be present. Alternatively, SLPE may represent a distinct psychotic disorder in which dysfunction is relatively confined to the temporal lobe. We compared people with SLPE, a control epileptic group and a primary schizophrenic group using technetium-99m hexamethylpropylene amine oxime single photon emission tomography (^{99m}Tc-HMPAO SPET) and a verbal fluency paradigm chosen to produce activation within temporal and prefrontal regions (Warburton *et al*, 1996). Our aim was to answer two questions. First, do people with SLPE show an excess of left temporal lobe dysfunction compared with non-psychotic epileptic controls? Second, do people with SLPE show prefrontal abnormalities similar to those reported in schizophrenia?

METHOD

Subjects and assessment schedules

There were three groups of subjects: (a) 12 subjects with chronic, interictal SLPE (SLPE group); (b) 16 people with epilepsy but no history of psychiatric illness (control epileptic group); (c) 11 people with schizophrenia but with no history of epilepsy (primary schizophrenic group). The subjects were recruited from in- and out-patient units of the Maudsley and Bethlem Royal Hospitals and the epilepsy outpatient clinic of King's College Hospital. Subjects in the two epileptic groups met diagnostic criteria for epilepsy (Gunn & Fenton, 1969) and were matched for clinical type of epilepsy (primary generalised or partial epilepsy) and laterality of seizure focus as determined by previous electroencephalogram (EEG) investigations. Subjects in the two psychotic groups met DSM–III–R criteria for schizophrenia (American Psychiatric Association, 1987). All three groups were matched for age, gender and parental socio-economic status. Exclusion criteria were age greater than 55 years, full scale IQ less than 70, history of drug or alcohol misuse, left handedness or the presence of gross structural pathology (for example, space occupying lesion) as determined by previous neuroimaging (computerised tomography, magnetic resonance imaging).

Demographic and clinical data relating to epilepsy and psychiatric history were recorded (see Table 1). Current psychiatric symptoms were assessed using the Brief Psychiatric Rating Scale (Overall & Gorham, 1962) immediately prior to scanning. Premorbid IQ was estimated using the National Adult Reading Test and the Schonell reading test (Schonell, 1942; Nelson, 1982). Subjects were asked to rate their own levels of anxiety on a 10-point visual analogue scale, before scanning and during each of the two cognitive tasks within the scanning session. All but one of the subjects with psychosis were taking neuroleptic medication, and all of the subjects with epilepsy were taking anticonvulsant medication, at the time of the scan.

Scanning procedure

Images reflecting regional cerebral blood flow (rCBF) were obtained following intravenous injection of ^{99m}Tc-HMPAO. A scanning electron microscope, single-slice, head-dedicated scanner was used to acquire the data on a 128 × 128 matrix, each pixel measuring 1.6 mm square. A split-dose technique (Shedlack *et al*, 1991) was employed to measure rCBF during the performance of a verbal fluency task and a control, word repetition, task. This technique allowed two sets of images to be taken within the same scanning session with the subject remaining in the scanner throughout. The advantage of this technique is that it facilitates the comparison of

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the first and second sets of images by minimising error due to repositioning of the subject. During each condition, images were acquired in two slice positions orientated parallel to the orbito-meatal plane; 3 cm and 5 cm above the orbito-meatal line. A total dose of 500 MBq ^{99m}Tc-HMPAO was administered to each subject through an intravenous cannula inserted in the antecubital vein. The ^{99m}Tc-HMPAO was divided into two doses, the first given during the word repetition task, the second given during the verbal fluency task. At the beginning of the study the split doses were 125/375 MBq respectively. However, with this administration schedule scanning times following the first dose were unacceptably long and, after eight subjects had been scanned in this way (three subjects each in the SLPE and epileptic control groups, two subjects in the schizophrenic group), the doses were changed to 250/250 MBq.

Immediately prior to scanning, subjects were given a trial of the verbal fluency task in which they were asked to produce as many words as possible beginning with the letter C. The number of responses given over one minute was recorded. The subject was then positioned in the scanner in a dimly lit room and allowed to rest for five minutes.

Table I Demographic and clinical characteristics of the three subject groups. Between group differences are not statistically significant unless otherwise indicated

	Group with SLPE	Control group with epilepsy	Group with schizophrenia
n	12	16	11
Gender male/female	6/6	10/6	8/3
Mean age (s.d.)	43.0 (9.7)	40.5 (9.7)	38.7 (10.4)
Mean premorbid IQ[1] (s.d.)	105.1 (14.1)	111.8 (9.9)	112.6 (6.4)
Parental Social Class[2]			
I–II	7	6	4
III	3	6	5
IV–V	2	4	2
Type of epilepsy			
Partial	10	14	–
Primary generalised	2	2	–
Mean duration epilepsy (years) (s.d.)	32.5 (10.4)	24.8 (12.2)	–
Mean seizure frequency[3] (s.d.)	30.2 (33.0)	25.4 (37.5)	–
Electroencephalogram laterality			
Left	5	6	–
Bilateral	2	0	–
Right	3	4	–
None	2	6	–
Mean duration psychosis (years) (s.d.)	13.5 (10.4)	–	24.8 (12.2)
Mean neuroleptic dose[4] (s.d.)	689 (703)	–	421 (570)
Mean Brief Psychiatric Rating Scale scores (s.d.)			
Positive symptoms	2.3 (3.7)	0	2.1 (2.8)
Negative symptoms	2.8 (3.2)	0	2.3 (2.8)
Total	5.5 (5.4)*	1.4 (2.3)	5.4 (5.2)*
Anxiety rating			
At baseline	2.2 (2.8)	2.6 (2.1)	4.6 (1.2)**
During word repetition	1.8 (2.0)	3.0 (2.5)	3.7 (2.0)
During word generation	4.4 (2.9)	3.3 (2.2)	4.4 (1.8)
Mean verbal fluency score (s.d.)	48.6 (29.9)	68.0 (30.2)	78.4 (22.9)***

1. National Adult Reading Test.
2. Registrar General's Socio-Economic Classification.
3. Number of seizures in previous year.
4. Chlorpromazine equivalents, mg per week.

*F=4.08, P=0.026; the two groups with psychoses had higher Brief Psychiatric Rating Scale scores than the control subjects with epilepsy but were not significantly different from one another. **F=3.89, P=0.031: the schizophrenic group had higher ratings of anxiety at baseline than the other two groups. ***F=3.37, P=0.046: schizophrenia-like psychosis of epilepsy (SLPE) group scored significantly lower than both the control subjects with epilepsy and the group with schizophrenia. There was no significant difference between scores of the subjects with epilepsy and schizophrenia.

Control (word repetition) task

The first set of images were acquired while subjects performed a word repetition task. In this task, subjects were given a word and asked to repeat it, over and over again. They were asked to do this slowly and a rate of approximately one repetition every three seconds was demonstrated to them by the investigator. One minute after being given the first word the subjects were presented with a second word and this process repeated for a total of six words (tulip, Monday, blue, kitten, February, gold) over six minutes. In designing the control task our intention was to match speech output in the control and verbal fluency tasks as closely as possible. For each subject the pre-scan trial of verbal fluency with the letter C provided an estimate of their expected performance in the verbal fluency task and this number was used to limit the number of times the subject repeated each word during the control task. Thus, after each word presentation the number of repetitions was recorded and the subject asked to stop, and to rest, once they reached the number of responses they had achieved in the pre-scan trial of verbal fluency. Where subjects had produced a large number of responses in the pre-scan trial of verbal fluency and did not reach that number of repetitions in the control task, they were simply asked to stop at the end of the minute allocated for that word and given the next word to repeat. The first dose of ^{99m}Tc-HMPAO was injected after the first minute of the task. Subjects were asked to keep their eyes closed and to remain as still as possible throughout the task. The first (control) scan was then performed.

Verbal fluency task

After the first set of images were acquired subjects were asked to remain in the same position within the scanner. They then performed a verbal fluency task in which they were given a letter and asked to say as many words as possible beginning with that letter. They were told that names (of people or places) were not allowed but that words

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with the same beginning but different endings were acceptable (bath, bathing, bather). After one minute they were asked to stop and were given a new letter. A total of six letters were given (F, A, S, P, R, W) and the responses recorded. The second dose of ^{99m}Tc-HMPAO was administered one minute into the task. As in the control condition, subjects were asked to keep their eyes closed and to remain still throughout the task.

Image analysis

Images were analysed on Strichman software using an AppleMac computer. Prior to analysis each scan was encoded so that the raters (J.M. & N.A.) were blind to subject identity, group membership and task condition. For each scan a cortical rim was delineated (see Fig. 1). First, a trace was drawn around the 60% isocontour of the brain to define the outer edge of the cortex. The inner boundaries of the cortical rim were then defined by moving the anterior and posterior poles of the outer trace inwards by eight pixels (lower slice) or six pixels (upper slice), and the lateral margins inwards by 12 (lower slice) or 10 pixels (upper slice). The cortical rim was then divided into six cortical regions on each side using a radial divider placed at the midpoint of the midsagittal line of each slice. To allow for the greater medial extent of temporal lobe cortex at the level of the lower slice, the inner boundary of this region was moved inwards by five pixels. Finally, a 10-pixel-wide strip was used to delineate parasagittal cortex in both upper and lower slices. The dimensions of the cortical strip and the construction of the radial divider were determined by reference to the Talairach & Tournoux atlas (1988). Interrater reliability of measurements made with this method was tested on five subjects (20 scans) and the intra-class correlation coefficient was found to exceed 0.85 for all regions of interest.

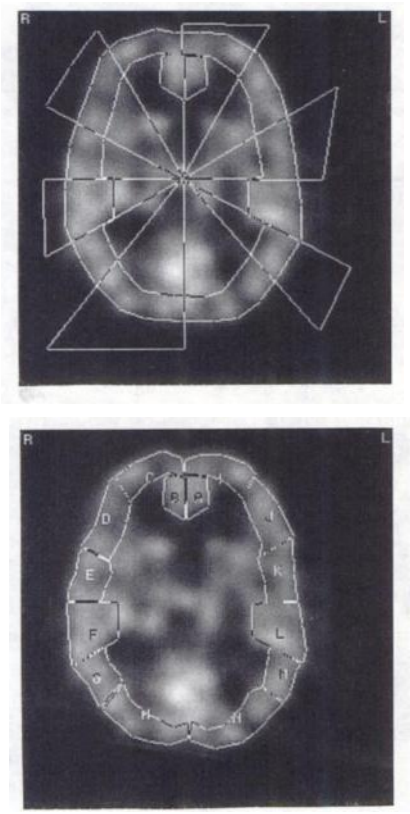

Fig. 1 SPET image from a single subject illustrating the method used to define cortical regions in the lower of the two slices acquired in the study. The top image illustrates the radial divider that was used to segment the cortical strip into regions of interest. The regions of interest are labelled in the lower image. Those included in the analysis were; A, B, anterior cingulate; C, I, frontal pole; D, J, prefrontal; K, E, frontal; F, L, superior temporal.

^{99m}Tc-HMPAO uptake was expressed as mean counts per pixel (count density). The count density in each region of interest was normalised to whole slice count density. Thus, the relative uptake within each cortical region of interest during the control (word repetition) task was expressed as the ratio of count density in each region of interest divided by whole slice count density.

In the verbal fluency task scan, the count density in each region of interest was corrected for ^{99m}Tc-HMPAO uptake remaining from the word repetition scan. Relative uptake during the verbal fluency task was thus expressed as the ratio of count density in each region of interest and whole slice count density, after subtracting the activity remaining from the word repetition scan. Percentages of rCBF increase associated with the verbal fluency task were also calculated for each region of interest.

Statistical analysis

Because of the large number of possible comparisons in this study, analyses were restricted to frontal and temporal lobe cortical regions. These were, in the lower slice-anterior cingulate, frontal pole, prefrontal, frontal and superior temporal cortex; and in the upper slice, anterior cingulate, prefrontal and temperoparietal cortex. Activity in these regions was first compared between groups during the word-repetition task using a multivariate analysis of variance (MANOVA). Next a repeated-measures MANOVA was performed with regional activity during word repetition and verbal fluency as the paired dependent measures, patient group as the between subject factor and cognitive task (word repetition/verbal fluency) as the within subject factor, before and after controlling for verbal fluency performance. *Post hoc* univariate tests were performed to examine between group differences on a region by region basis. The relationship between clinical variables and percentage increase in regional brain activity was examined using Pearson's correlation coefficient. Excluding the eight subjects who were scanned with the initial split-dose ratio of 125/375 MBq made no difference to the interpretation of the results and they are therefore included in the final analyses presented here.

RESULTS

Clinical data and verbal fluency performance

A summary of demographic, clinical and verbal fluency performance data is presented in Table 1. The subjects' in the group SLPE performance of the verbal fluency task was significantly worse than the other two groups.

Differences in rCBF between groups

There were no significant differences between subject groups in regional brain activity during word repetition (Table 2). Combining data from all subjects, verbal fluency compared with word repetition was associated with a significant increase in anterior cingulate (BA 32) activity ($F=4.96$; $P=0.032$). Activation was also seen in the left dorsolateral prefrontal cortex during verbal fluency but this fell short of statistical significance ($F=3.27$, $P=0.08$). Turning to the repeated measures MANOVA analysis, activation in two regions, both in the lower slice, were significantly different between groups: first, the primary schizophrenic group showed greater activation of the anterior cingulate than the other two groups ($F=6.28$; $P=0.005$); second, the people with SLPE showed less activity in the left superior temporal cortex during

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Table 2 Mean (s.d.) regional activity in the three subject groups

Region of interest	Group with SLPE		Control group with epilepsy		Group with primary schizophrenia	
	R word repetition	R verbal fluency	R word repetition	R verbal fluency	R word repetition	R verbal fluency
Lower slice						
Anterior cingulate	2.13 (0.29)	2.15 (0.30)	2.26 (0.15)	2.28 (0.18)	2.07 (0.30)	2.39(0.31)[1]
Frontal pole (L)	1.05 (0.09)	1.03 (0.11)	1.09 (0.04)	1.07 (0.07)	1.03 (0.11)	1.13 (0.14)
Frontal pole (R)	1.01 (0.09)	1.00 (0.15)	1.08 (0.05)	1.02 (0.08)	1.04 (0.11)	1.07 (0.15)
Prefrontal (L)	1.05 (0.06)	1.07 (0.08)	1.07 (0.06)	1.11 (0.06)	1.06 (0.10)	1.07 (0.11)
Prefrontal (R)	1.06 (0.07)	1.07 (0.08)	1.10 (0.05)	1.09 (0.06)	1.08 (0.09)	1.08 (0.09)
Frontal (L)	1.06 (0.04)	1.09 (0.11)	1.07 (0.05)	1.11 (0.08)	1.06 (0.06)	1.07 (0.05)
Frontal (R)	1.12 (0.06)	1.07 (0.10)	1.11 (0.06)	1.08 (0.10)	1.09 (0.07)	1.03 (0.08)
Superior temporal gyrus (L)	1.10 (0.06)	1.01 (0.08)[2]	1.10 (0.07)	1.11 (0.08)	1.10 (0.05)	1.12 (0.08)
Superior temporal gyrus (R)	1.11 (0.07)	1.08 (0.08)	1.14 (0.06)	1.13 (0.09)	1.12 (0.08)	1.10 (0.05)
Upper slice						
Anterior cingulate	1.91 (0.36)	1.75 (0.80)	2.08 (0.19)	2.05 (0.15)	1.97 (0.31)	2.05 (0.30)
Prefrontal (L)	1.09 (0.06)	1.03 (0.17)	1.08 (0.07)	1.05 (0.07)	1.06 (0.04)	1.05 (0.07)
Prefrontal (R)	1.10 (0.04)	1.07 (0.16)	1.10 (0.04)	1.10 (0.07)	1.07 (0.05)	1.09 (0.09)
Frontal (L)	1.09 (0.06)	1.08 (0.20)	1.10 (0.06)	1.09 (0.05)	1.08 (0.05)	1.13 (0.09)
Frontal (R)	1.13 (0.06)	1.12 (0.09)	1.10 (0.06)	1.08 (0.10)	1.10 (0.06)	1.15 (0.08)
Temperoparietal (L)	1.10 (0.08)	1.13 (0.17)	1.12 (0.08)	1.09 (0.10)	1.10 (0.08)	1.12 (0.07)
Temperoparietal (R)	1.16 (0.10)	1.13 (0.11)	1.16 (0.06)	1.12 (0.08)	1.11 (0.07)	1.13 (0.07)

R, mean ratio of count density for each region normalised to whole slice count density; results of MANOVA for repeated measures: for lower slice, no main effect of group or condition, trend for main effect of group by condition interaction (F=1.73, P=0.059); for upper slice, no main effects of group, condition or group by condition interactions. *Post hoc* univariate F-tests (lower slice only).

1. Subjects with schizophrenia showed increased activation in the anterior cingulate than the other two groups, F=5.73, P=0.007.

2. Subjects with schizophrenia-like psychosis of epilepsy (SLPE) showed a relative decrease in activation within the left superior temporal region which was significantly different from the other two groups, F=6.18, P=0.005.

verbal fluency compared with word repetition, this differing significantly from the situation observed in the other two groups (F=6.69; P=0.004). Both of these differences remained significant after controlling for verbal fluency performance (F=6.49, P=0.004 and F=6.34, P=0.028 respectively). To investigate the relationship between laterality of EEG abnormalities and SPET data, analyses were repeated for the superior temporal lobe regions of interest including only the SLPE and control subjects with epilepsy with lateralised EEG findings. Grouping the psychotic and non-psychotic subjects with epilepsy together, there were no significant differences in activation between those subjects with left and those with right-sided EEG abnormalities. The difference in left superior temporal activation between the SLPE and the control epileptic groups remained significant after controlling for laterality of EEG findings (F=7.747, P=0.005).

Relationship between rCBF and clinical measures

Across all subjects verbal fluency performance was correlated negatively with left prefrontal activation (r=−0.32, P=0.048). Within groups, there were no significant correlations between verbal fluency score and tracer uptake. There was no relationship between activation and neuroleptic medication or measures of anxiety.

DISCUSSION

SLPE group

The main experimental measure in the present study was the difference between SPET tracer uptake during a verbal fluency and a control (word repetition) task. In normal subjects similar activation paradigms are associated with an increase in regional cerebral blood flow within the left prefrontal and anterior cingulate cortices and with either an increase or a decrease within the left superior temporal cortex. The variability in superior temporal lobe response between studies is probably related to differences in the control tasks with which verbal fluency is compared (Warburton *et al*, 1996).

Subjects with SLPE differed from both the non-psychotic epileptic control group and the group with primary schizophrenia by showing less activity within the left temporal lobe during the fluency task compared with the control task. While the control group with epilepsy and the subjects with primary schizophrenia showed similar levels of left temporal lobe activity during both tasks, the SLPE group showed a relative decrease in uptake within this region during performance of the verbal fluency task. It is unlikely that this finding is attributable to between group differences in task performance, as the experimental procedure was designed to control for speech output and the difference in tracer uptake remained significant after controlling for verbal fluency scores. Neuroleptic medication is also unlikely to account for this finding as the SLPE group had significantly less left temporal lobe tracer uptake than the subjects with primary schizophrenia and both groups were receiving similar doses of neuroleptics.

There were no other significant differences between the subjects with SLPE and the non-psychotic epileptic control group. In particular, there were no differences in prefrontal tracer uptake between these two groups. Our results therefore not only implicate dominant temporal lobe dysfunction

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in SLPE but, within the limits of the sensitivity of the SPET technique that we have used, they suggest that such dysfunction, if extensive enough, may be sufficient to place a person with epilepsy at risk of developing schizophrenia.

Early studies reporting an association between left temporal lobe epileptic foci and SLPE have not been replicated by a number of carefully designed electroencephalographic and structural (CT) scanning studies (Kristensen & Sindrup, 1978; Toone *et al*, 1982; Mendez *et al*, 1993). Such inconsistencies may partly be due to the use of techniques that have sought to establish the laterality of epileptic activity or the presence of gross structural abnormalities. Disruption of brain function in patients with epilepsy is known to extend beyond the epileptogenic lesion itself and to persist well after the immediate post-ictal period (Devous *et al*, 1990). Although structural, electrophysiological and functional abnormalities in epilepsy are clearly related, it seems likely that interictal psychiatric disorders, including SLPE, are most closely linked to abnormalities of brain function that persist between seizures. SPET therefore has an important advantage over previous methods in that it examines interictal brain function. Our finding of an excess of left temporal lobe dysfunction in the SLPE group compared with the control group with epilepsy occurred even though the two groups were matched for laterality of epileptic focus as indicated by previous EEGs. Furthermore, the left temporal difference between people with SLPE and the control group with epilepsy remained significant when a subgroup of subjects with unilateral EEG abnormalities was examined controlling for laterality of EEG findings. There was therefore some evidence that the left temporal SPET abnormality was independent of seizure focus. However, scalp EEG provides relatively poor lateralising information and the subject numbers in the current study are too small to permit firm conclusions. Our findings are consistent with those of Marshall *et al* (1993), who obtained resting SPET images from five subjects with SLPE and control subjects with epilepsy who were also matched for laterality of EEG abnormalities. As in our study, Marshall *et al* found an excess of left temporal dysfunction in the subjects with SLPE.

Our results and those of Marshall *et al* also agree in finding no differences in frontal lobe function between the psychotic and non-psychotic groups with epilepsy. Tracer uptake within the frontal regions was similar in all three groups in the current study. In the absence of a normal control group we cannot conclude that frontal function was normal in all subjects. However, we can infer that if such dysfunction was present then it was found to an equal extent in all three groups and was therefore not specifically associated with psychosis, either in the group suffering from primary schizophrenia or in the subjects with SLPE. 'Hypofrontality' in schizophrenia has proved an inconsistent finding, both when brain function is examined at rest and during activation (Chua & McKenna, 1995). In relation to activation studies, it may be that if some method of standardising or controlling for task performance is employed then frontal abnormalities are not found (Frith *et al*, 1995).

Primary schizophrenic group

The subjects with primary schizophrenia differed from both epileptic groups by showing a greater tracer uptake within the anterior cingulate while they performed the verbal fluency task. As mentioned previously, without a normal control group we cannot be certain whether this finding represents an abnormality in the groups with schizophrenia or epilepsy. A study by Dolan *et al* (1995) provides some support for interpreting the anterior cingulate findings as an abnormality in the group with schizophrenia. Dolan *et al* found increased anterior cingulate activation during verbal fluency in neuroleptic-free subjects with schizophrenia compared with healthy controls following the administration of low-dose apomorphine. We might be observing a similar effect in our medicated subjects with primary schizophrenia.

Limitations

A number of methodological issues need to be considered. First, the inclusion of a normal control group would have allowed us to establish the normal pattern of activation with the tasks used in our study but this was not possible for ethical reasons: to have matched a normal control group with the subjects would have entailed scanning healthy women of reproductive age. Our results are thus limited to comparisons between groups and we cannot be certain where deviations from normality lie. This is of particular importance in relation to the findings in the subjects with schizophrenia. For example, while tracer uptake within the left temporal lobe was similar in the schizophrenia and the epilepsy control groups, this may represent an abnormality in both groups. Second, no attempt was made to standardise performance of the verbal fluency task between the three groups. We chose not to follow the method of pacing the fluency task that others have advocated (Frith *et al*, 1995) as we believe that to have done so would have removed an important component of the verbal fluency task itself; namely, the sustained effort (without metronomic cues) involved in generating novel verbal responses that meet a prescribed constraint. Instead, the word repetition and fluency tasks were tailored in each individual to control for speech output. The negative correlation between verbal fluency performance and left prefrontal tracer uptake provides some internal validation of our method and is consistent with the inverse relationship between performance and rCBF reported by others for executive tasks involving frontal cortex (Kawasaki *et al*, 1993). Other aspects of the study design may have reduced the sensitivity of our method, these include the region of interest-based image analysis, and the possibility of an order effect (and a group by order effect) inherent in the split-dose method of activation task presentation. Finally, our findings with respect to the laterality of temporal lobe dysfunction must be interpreted with caution. Although no differences were observed on the right side, the verbal fluency task would not have been expected to produce activation within the nondominant hemisphere and our experimental design was therefore intrinsically more sensitive to left rather than right sided abnormality.

CONCLUSION

Our study adds to previous evidence suggesting an association between left temporal lobe dysfunction and the development of schizophrenia-like psychoses in people with epilepsy. We found no evidence of prefrontal deficits either in subjects with SLPE or in those with primary schizophrenia when compared with a control group of non-psychotic subjects with epilepsy. Subjects with schizophrenia and SLPE showed significantly different patterns of activation, suggesting that the

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brain abnormalities underlying these two disorders may be different: in SLPE the pathophysiology appears to lie principally within the left temporal lobe, while primary schizophrenia may be associated with functional abnormalities of the anterior cingulate. Although our findings highlight abnormality of the anterior cingulate in schizophrenia, this must be interpreted with caution as we did not study a normal control group and we chose a paradigm which activated this region. Compelling evidence elsewhere suggests that schizophrenia is associated with widespread brain abnormalities, possibly of neurodevelopmental origin (Ron & Harvey, 1990).

CLINICAL IMPLICATIONS

- The present study supports an association between left-sided temporal lobe abnormality and the schizophrenia-like psychoses of epilepsy (SLPE).
- The study failed to find evidence of prefrontal abnormalities associated with schizophrenia, either in SLPE or in primary schizophrenia.
- The study suggests that the pathophysiology of the SLPE may be different from that of primary schizophrenia.

LIMITATIONS

- The study lacked a normal control group. Analyses were restricted to comparisons between subject groups and deviations from normality could not be defined.
- Non-standard verbal fluency activation paradigm means that results cannot easily be compared with previous studies.
- By using a verbal fluency activation paradigm, the study was intrinsically more sensitive to left rather than right-sided differences between groups.

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