Handedness, language lateralisation and anatomical asymmetry in schizophrenia

Meta-analysis

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Background Cerebral lateralisation appears to be decreased in schizophrenia. Results of studies investigating this, however, are equivocal.

Aims To review quantitatively the literature on decreased lateralisation in schizophrenia.

Method Meta-analyses were conducted on 19 studies on handedness, 10 dichotic listening studies and 39 studies investigating anatomical asymmetry in schizophrenia.

Results The prevalence of mixed- and left-handedness ('non-right-handedness') was significantly higher in patients with schizophrenia as compared to healthy controls, and also as compared to psychiatric controls. The analysis of dichotic listening studies revealed no significant difference in lateralisation in schizophrenia. However, when analysis was restricted to studies using consonant–vowel or fused word tasks, significantly decreased lateralisation in schizophrenia emerged. Asymmetry of the planum temporale and the Sylvian fissure was significantly decreased in schizophrenia, while asymmetry of the temporal horn of the lateral ventricle was not.

Conclusion Strong evidence is provided for decreased cerebral lateralisation in schizophrenia.

Declaration of interest None

Right-handedness, left cerebral dominance for language and normal cerebral asymmetry are considered to be secondary to a dominant allele, the 'right-shift factor' (Annett, 1998). In schizophrenia, several studies reported an excess of non-right-handedness (Shan-Ming *et al*, 1985), decreased language lateralisation on the dichotic listening paradigm (Bruder *et al*, 1999) and decreased (Petty *et al*, 1995) or reversed (Barta *et al*, 1997) anatomical asymmetry. It has been postulated that the genetic mechanism underlying normal left hemispheric dominance is altered in schizophrenia (Crow *et al*, 1989). Were this to be true, the discovery of the 'right-shift factor' may also identify a locus where genetic aberrations predispose for schizophrenia (Crow, 1999). However, literature on decreased cerebral dominance in schizophrenia is equivocal. The aim of the present study was therefore to review quantitatively studies on handedness, language lateralisation on the dichotic listening paradigm and anatomical asymmetry in schizophrenia.

METHOD

Literature search

Studies were retrieved that dealt with lateralisation in schizophrenia, published between January 1980 (introduction of *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn), DSM–III) and December 1999. Only English-language publications from international journals and book chapters were selected.

Inclusion

The included studies had to meet the following criteria.

(a) Patients had a diagnosis of schizophrenia, according to the criteria of DSM–III, DSM–III–R, DSM–IV, Research Diagnostic Criteria (RDC), International Classification of Disease ICD–9 or ICD–10. Studies on patients with schizophrenia-spectrum disorder (schizoaffective and schizophreniform disorder or schizotypal personality disorder) were not included.

(b) Studies had compared patients with schizophrenia to healthy controls who were not at increased risk for schizophrenia or psychosis. For an additional analysis on hand preference, we also included studies using non-schizophrenia psychiatric and neurological patients as control groups.

(c) Studies reported data on handedness, language lateralisation as measured with the dichotic listening paradigm, or anatomical asymmetry of the planum temporale, Sylvian fissure, temporal horn of the lateral ventricle or superior temporal gyrus.

(d) Studies had reported sufficient statistical information, i.e. frequencies, means and standard deviations, exact F or t values, or exact P values.

Analyses

After computing effect sizes for each study (Hedges & Olkin, 1985), meta-analytic methods were applied in order to obtain a combined effect size, which indicated the magnitude of the association across all studies (cf Aleman *et al*, 1999). In addition, Stouffer's Z, weighted for sample size, provided an indication of the significance of the difference between the patient and the comparison group. Finally, a homogeneity statistic (Q) was calculated, to assess heterogeneity of results across studies (Shadish & Haddock, 1994). If heterogeneity reached significance, further analyses were carried out to examine potential moderators on the effect size. In order to investigate such potential moderators, correlations (Pearson coefficients, two-tailed) were calculated between the effect size of the studies and available variables.

Handedness

Prevalences of mixed- and left-handedness were grouped together as 'non-right-handedness'. For each study, odds ratios were calculated from the prevalence of non-right-handedness in schizophrenia or pre-schizophrenia subjects and in the comparison subjects. Odds ratios were combined by applying the method of logarithmic odds ratio meta-analysis (Shadish & Haddock, 1994).

Dichotic listening studies

Effect sizes (Hedges & Olkin, 1985) were calculated from the 'right-ear advantages' (score right ear minus score left ear) of patients and controls, from the 'laterality index' (score right ear minus score left ear, divided by score right ear plus score left ear) or from *F* values.

Anatomical asymmetry

Brain torque

Only two studies on brain torque (Luchins *et al*, 1981; Guerguerian & Lewine, 1998) reported means and standard deviations of an asymmetry index for patients and controls, while others gave frequencies of abnormal frontal and occipital asymmetry. On these studies, meta-analysis was performed using the 'difference rate', i.e. the difference between the proportion of individuals with absent or reversed asymmetry in the patient group and in the control group. For the meta-analyses on asymmetry of the planum temporale, Sylvian fissure, temporal horn of the lateral ventricle and superior temporal gyrus, effect sizes were computed from the mean size (and standard deviation) of left and right structures. The measurements concerned absolute structure sizes, not corrected for total brain volume, and total structure sizes (not only grey matter volumes). When studies gave separate data for men and women, these were included as two independent effect sizes, thereby increasing the total number of effect sizes (*K*).

Each study was used for three meta-analyses. In the first, asymmetry of the structure was calculated for the control subjects. In the second, asymmetry was calculated for the patients. The third meta-analysis was conducted on the difference of the two *d* values of each group and compared asymmetry in patients to that in controls. In this way, differences in overall brain size between patients and controls could not influence the outcome, as every structure was compared to its contralateral homologue first, after which the resulting standardised asymmetry indices were compared between the groups. Differences in measurement technique between the studies were largely controlled for, as well as the statistic results from within-study comparisons.

When studies that measured the superior temporal gyrus provided separate data on anterior, middle and posterior segments, these were pooled.

All studies had included predominantly right-handed subjects, except for Holinger *et al* (1999), who measured superior temporal gyral volumes in left-handed patients with schizophrenia and left-handed controls. To increase homogeneity among studies, this study was excluded in the meta-analysis, but included for the calculation of a possible correlation between handedness distribution and asymmetry.

RESULTS

Handedness

Sixteen cross-sectional studies that assessed handedness in patients with schizophrenia and healthy subjects were included (Taylor *et al*, 1980; Chaugule & Master, 1981; Piran *et al*, 1982; Kameyama *et al*, 1983; Manschreck & Ames, 1984; Merrin, 1985; Shan-Ming *et al*, 1985; Green *et al*, 1989; Nelson *et al*, 1993; Clementz *et al*, 1994; Cannon *et al*, 1995; Green & Rieg, 1995; O'Callaghan *et al*, 1995; Taylor & Amir, 1995; Malesu *et al*, 1996; Orr *et al*, 1999).

Meta-analysis on these studies showed that the prevalence of non-right-handedness was significantly higher in patients with schizophrenia than in healthy subjects (Table 1). The magnitude of the odds ratios of each study is shown in Fig. 1.

Three prospective follow-up studies measured hand preference in children of large birth cohorts, who were screened for schizophrenia in adult life (David *et al*, 1995; Crow *et al*, 1996; Cannon *et al*, 1997). From these, only one study (Crow *et al*, 1996) provided quantitative indices on the degree of handedness. In the meta-analysis of these studies, pre-schizophrenic subjects were significantly more often non-right-handed than were the general population (Table 1).

Additional analysis was performed on nine studies where the comparison group

Table 1 Summary of meta-analyses of difference in cerebral dominance between patients with schizophrenia and comparison subjects

Index	*K*	*N*	*D*	OR	DR	95% CI	*Z* (*P*)	*Q* (*P*)
Handedness								
Patients with schizophrenia *v.* healthy controls	16	5467		1.61		1.41–1.81	3.69 (0.0002)	23.6 (0.13)
Patients with schizophrenia *v.* psychiatric controls	9	1492		1.54		1.28–1.84	2.36 (0.009)	11.46 (0.2)
Prospective	3	55 579		1.48		1.23–1.79	2.07 (0.02)	2.24 (0.31)
Dichotic listening								
All verbal tasks	10	434	−0.19			−0.6–0.2	−0.92 (0.18)	29.2 (0.001)
Only CV and fused-words	6	267	−0.48			−0.83 to −0.14	12.74 (0.003)	8.9 (0.11)
Anatomical asymmetry								
Frontal torque	3	383			0.24	0.15–0.34	5.11 (0.05)	8.4 (0.05)
Occipital torque	5	579			0.22	0.12–0.28	7.59 (0.01)	87.55 (0.003)
Planum temporale	11	368	−0.51			−1.04–0.02	−1.87 (0.03)	54.5 (0.0005)
Sylvian fissure	3	185	−0.62			−1.04–0.2	−2.87 (0.002)	11.1 (0.03)
Temporal horn lateral ventricle	12	629	−0.11			−0.61–0.4	−0.41 (0.34)	106.83 (0.0001)
Superior temporal gyrus	17	1020	0.21			−0.08–0.51	1.41 (0.08)	93.3 (0.0001)
Posterior segment STG	5	238	0.7			0.4–1	6.3 (0.0001)	5.42 (0.37)

K, number of effect sizes; *N*, number of subjects; *D*, mean weighted effect size; OR, mean weighted odds ratio; DR, mean weighted difference rate; CV, consonant–vowel; STG, superior temporal gyrus; Z, Stouffer's Z.

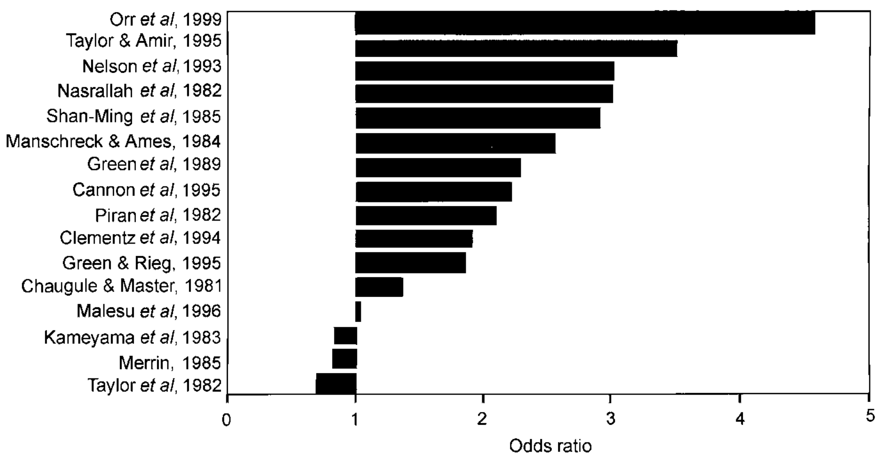

Fig. 1 Odds ratios of non-right-handedness in schizophrenia.

consisted of non-schizophrenia psychiatric or neurological patients (Chaugule & Master, 1981; Piran *et al*, 1982; Manschreck & Ames, 1984; Merrin, 1985; Shan-Ming *et al*, 1985; Clementz *et al*, 1994; Taylor & Amir, 1995; Malesu *et al*, 1996; Orr *et al*, 1999). The results indicated that the prevalence of non-right-handedness was significantly higher in schizophrenia subjects than in other psychiatric and neurological patients (Table 1).

Dichotic listening studies

Meta-analysis was conducted on 10 dichotic listening studies that compared patients with schizophrenia to healthy controls (Hatta *et al*, 1984; Wexler *et al*, 1991; Carr *et al*, 1992; Ragland *et al*, 1992; Seidman *et al*, 1993; Grosh *et al*, 1995; Sakuma *et al*, 1996; Oie *et al*, 1998; Bruder *et al*, 1999; Løberg *et al*, 1999). The right-ear advantage was not significantly decreased in schizophrenia, with significant heterogeneity among studies (Table 1). The magnitude of the effect size of each study is represented in Fig. 2.

A possible cause for the inhomogeneity in these studies may be the difference in verbal tasks the studies used to elicit a right-ear advantage. Four different tasks were used: the triad task, the fused-word task, the consonant–vowel task and the word-monitoring task. The fused-word and the consonant–vowel tasks are considered to reflect cerebral dominance most accurately (see Discussion). When only studies that used the fused-word and the consonant–vowel tasks were included, the right-ear advantage was significantly lower in schizophrenia and studies were no longer heterogeneous (Table 1).

Anatomical asymmetry

Brain torque

Meta-analyses were conducted on the frequency of abnormal asymmetry of the frontal lobe (Andreasen *et al*, 1982; Jernigan *et al*, 1982; Falkai *et al*, 1995*b*) and the occipital lobe (Andreasen *et al*, 1982; Jernigan *et al*, 1982; Luchins & Meltzer, 1983, 1986; Falkai *et al*, 1995*b*). The results showed that the frequency of abnormal asymmetry was significantly higher in schizophrenia for both the frontal and the occipital lobe, but studies were heterogeneous (Table 1). The small number of studies allowed no further investigation of potential moderators.

Planum temporale

Meta-analysis was performed on 10 studies that measured the planum temporale in schizophrenia (Rossi *et al*, 1992, 1994; Kleinschmidt *et al*, 1994; Falkai *et al*, 1995*a*; Kulynych *et al*, 1995; Petty *et al*, 1995; Jacobsen *et al*, 1996; Barta *et al*, 1997; Frangou *et al*, 1997; Kwon *et al*, 1999). In the meta-analysis, significant asymmetry favouring the left hemisphere was found for the healthy comparison subjects, but not for the patients (Table 2). Studies were homogeneous for the comparison subjects, but heterogeneous for the patients, indicating that difference in measurement technique is not a factor. Possible moderators may be found in characteristics of the patient samples. Only three variables were reported frequently enough to calculate correlations, but no significant result emerged: gender distribution $n=10$, $r=-0.25$, NS; handedness distribution $n=9$, $r=0.38$, NS; duration of illness $n=6$, $r=-0.29$, NS.

In the meta-analysis directly comparing patients and controls, asymmetry of the planum temporale was significantly reduced in patients (Table 1). The magnitude of the difference in effect sizes of asymmetry between patients and controls is shown in Fig. 3.

Sylvian fissure

In the meta-analysis on studies on asymmetry of the Sylvian fissure (Falkai *et al*, 1992; Hoff *et al*, 1992; Bartley *et al*, 1993), both controls and patients showed significant asymmetry favouring the left hemisphere (Table 2), but studies were heterogeneous for both groups. The small number of studies allowed no further investigation of potential moderators. When asymmetry of the Sylvian fissure was directly compared between patients with schizophrenia and healthy subjects, patients showed significantly decreased asymmetry (Table 1).

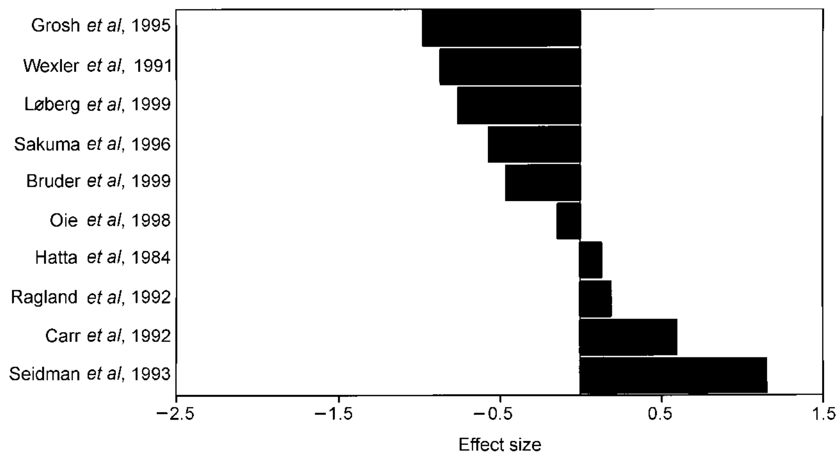

Fig. 2 Effect sizes of dichotic listening studies in schizophrenia (patients−controls).

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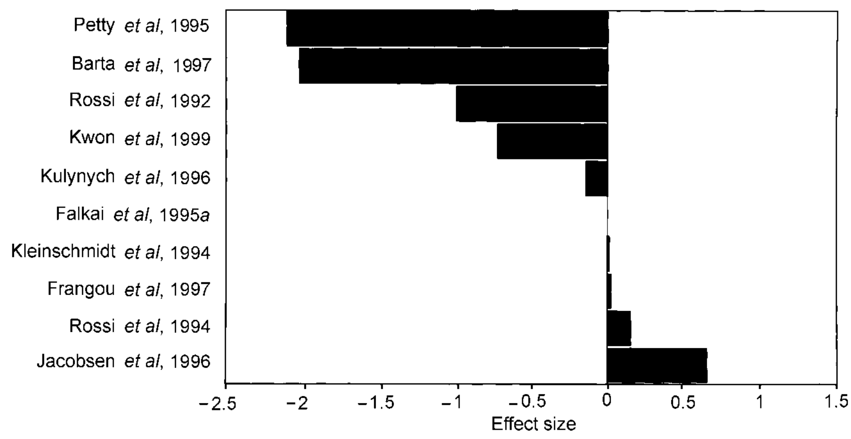

Fig. 3 Difference in asymmetry (patients–controls) of the planum temporale.

Temporal horn of the lateral ventricle

Eight studies on asymmetry of the temporal horn of the lateral ventricle were included (Bogerts *et al*, 1990; Dauphinais *et al*, 1990; DeLisi *et al*, 1991; Zipursky *et al*, 1994; Flaum *et al*, 1995; Becker *et al*, 1996; Marsh *et al*, 1997; Pearlson *et al*, 1997). In healthy as well as in schizophrenia subjects, rightward asymmetry was found (Table 2). Studies were homogeneous for the analysis of control subjects, but heterogeneous in the patients' analysis (Table 2). Correlations between asymmetry in patients and possible moderators were not significant: gender distribution n=8, r=−0.44, NS; handedness distribution n=5, r=0.27, NS; duration of illness n=6, r=−0.7, NS. In the meta-analysis directly comparing patients and controls, asymmetry of the temporal horn was not significantly different between schizophrenia and healthy subjects (Table 1).

Superior temporal gyrus

Meta-analysis was performed on 15 studies measuring superior temporal gyrus in schizophrenia subjects and healthy controls (Barta *et al*, 1990; Zipursky *et al*, 1994; Flaum *et al*, 1995; Menon *et al*, 1995; Vita *et al*, 1995; Kulynych *et al*, 1996; Frangou *et al*, 1997; Marsh *et al*, 1997; Pearlson *et al*, 1997; Reite *et al*, 1997; Hirayasu *et al*, 1998; Jacobsen *et al*, 1998; Bryant *et al*, 1999; Havermans *et al*, 1999; Highley *et al*, 1999).

The results showed that the superior temporal gyrus was larger in the right hemisphere in schizophrenia subjects, while controls showed a trend towards asymmetry in the same direction (Table 2). Studies were heterogeneous for both groups and thus differences in measurement technique may have acted as moderators. The only study on post-mortem brains (Highley *et al*, 1999) found larger volumes of the superior temporal gyrus in the left hemisphere in controls, while 13 of 14 magnetic resonance imaging (MRI) studies found larger volumes in the right hemisphere in controls. However, when the post-mortem study was excluded from analysis, heterogeneity among studies remained high. Correlations between the effect size of asymmetry in controls and other potential moderators were not significant (slice and gap thickness n=15, r=−0.039, NS; sample size n=15, r=−0.22, NS; gender distribution n=15, r=−0.29, NS; handedness distribution n=15, r=0.32, NS). Correlations between potential moderators and the effect size of asymmetry in patients were not significant either (slice and gap thickness n=15, r=0.15, NS; sample size n=15, r=−0.18, NS; gender distribution n=15, r=−0.27, NS; handedness distribution n=15, r=−0.29, NS; duration of illness n=5, r=−0.51, NS).

In the meta-analysis directly comparing patients and controls, the patients with schizophrenia tended to have increased asymmetry of the superior temporal gyrus favouring the right hemisphere, but statistical significance was not reached (Table 1).

Posterior segment of the superior temporal gyrus

A separate analysis on five studies (Menon *et al*, 1995; Kulynych *et al*, 1996; Pearlson *et al*, 1997; Hirayasu *et al*, 1998; Jacobsen *et al*, 1998) was performed to assess asymmetry of the posterior segment of the superior temporal gyrus. Rightward asymmetry was found for the patients, while the controls showed a trend towards asymmetry

Table 2 Summary of meta-analyses of difference in size between left and right hemispheric structures in controls and patients

Index	*K*	*N*	*D*	95% CI	*Z* (*P*)	*Q* (*P*)
Healthy controls						
Planum temporale	11	187	0.7	0.49–0.91	6.5 (0.00001)	4.3 (0.89)
Sylvian fissure	3	100	0.87	0.43–1.32	3.86 (0.00006)	9.85 (0.04)
Temporal horn lateral ventricle	12	303	−0.25	−0.41 to −0.09	−3.05 (0.001)	9.32 (0.59)
Superior temporal gyrus	17	399	−0.47	−1.1–0.14	−1.5 (0.07)	140.23 (0.0001)
Posterior segment STG	5	130	−0.2	−0.44–0.05	−1.58 (0.06)	1.5 (0.9)
Patients with schizophrenia						
Planum temporale	11	181	0.18	−0.33–0.69	0.7 (0.24)	48.7 (0.001)
Sylvian fissure	3	97	0.31	−1.04–0.2	2.87 (0.002)	4.72 (0.32)
Temporal horn lateral ventricle	12	324	−0.42	−0.88 to −0.04	−1.81 (0.04)	92.5 (0.00001)
Superior temporal gyrus	17	469	−0.73	−1.2 to −0.25	−2.95 (0.0016)	151.7 (0.0001)
Posterior segment STG	5	108	−0.9	−0.17 to −0.62	−6.23 (0.00001)	4.85 (0.43)

K, number of effect sizes; *N*, number of subjects; *D*, mean weighted effect size; *Z*, Stouffer's *Z*; *Q*, within-category homogeneity statistic; STG, superior temporal gyrus.

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in the same direction (Table 2). In the meta-analysis directly comparing patients and controls, rightward asymmetry of the posterior segment of the superior temporal gyrus was significantly larger in patients (Table 1).

DISCUSSION

The purpose of this study was to summarise present literature on cerebral dominance in schizophrenia quantitatively. The resulting analyses showed that functional asymmetry is decreased in schizophrenia, which was reflected in an increased prevalence of non-right-handedness and decreased language lateralisation in dichotic listening studies that applied the fused-word or consonant–vowel task. Decreased structural asymmetry in schizophrenia was found for brain torque, the planum temporale and Sylvian fissure, but not for the temporal horn of the lateral ventricle.

Hand preference

In the meta-analysis on handedness in cross-sectional studies, schizophrenia subjects were more frequently non-right-handed than healthy persons. However, these studies mainly included hospitalised patients with schizophrenia, thus tending to overrepresent severe cases. Prospective cohort studies do not have this limitation, since they are population-based. In the meta-analysis on three prospective cohort studies, the prevalence of non-right-handedness in subjects that later developed schizophrenia was significantly increased.

However, many diseases that involve subtle brain damage may be accompanied by increased prevalence of non-right-handedness (Satz & Green, 1999). To investigate the specificity of increased non-right-handedness in schizophrenia, an additional analysis was conducted comparing schizophrenia patients with non-schizophrenia psychiatric and neurological patients. In that analysis, non-right-handedness was still significantly increased in schizophrenia, suggesting that a specific cerebral lesion cannot explain the increased prevalence of non-right-handedness in schizophrenia. Thus, a more fundamental, possibly genetic mechanism may be involved. Interestingly, several studies report increased non-right-handedness in healthy relatives of patients with schizophrenia (Hallett *et al*, 1986; Chapman & Chapman, 1987; Orr *et al*, 1999), suggesting a genetic cause for decreased cerebral dominance in schizophrenia (Crow *et al*, 1989).

Dichotic listening studies

In the analysis of dichotic listening studies, the right-ear advantage was not significantly decreased in schizophrenia, while heterogeneity among studies was high. This may be attributable to the differences in verbal tasks used to elicit a right-ear advantage. For the triad task and the word-monitoring task, subjects have to respond to all stimuli on either ear. Schizophrenia subjects generally have a lower performance on these tasks than healthy subjects (Hatta *et al*, 1984; Carr *et al*, 1992; Seidman *et al*, 1993; Sakuma *et al*, 1996). On several items of these tasks, controls may have 100% correct response, in which case no perceptual asymmetry is measured. These ceiling effects in the control, but not in the schizophrenia group, may cause relatively low ear asymmetry in the control group. For the consonant–vowel and the fused-word tasks, subjects were asked to respond only to the most clearly perceived item, thereby avoiding the problem of ceiling effects. When only studies that applied the consonant–vowel or fused-word task were included, patients with schizophrenia showed a significantly decreased right-ear advantage and heterogeneity disappeared. A decreased right-ear advantage was also reported in healthy parents (Grosh *et al*, 1995) and children (Hallett *et al*, 1986) of patients with schizophrenia, supporting the hypothesised genetic origin of decreased lateralisation in schizophrenia.

Anatomical asymmetry

In the meta-analysis of anatomical studies, the direction of brain torque was more frequently inverted, while the planum temporale and Sylvian fissure showed reduced asymmetry in schizophrenia. The decreased temporo-parietal asymmetries probably reflect decreased language dominance, since planum temporale and Sylvian fissure asymmetries are strongly related to cerebral dominance (Gerschlager *et al*, 1998). Shapleske *et al* (1999) published an extensive review on the planum temporale that also contained a meta-analysis on the planum temporale in schizophrenia. The present study, using more stringent inclusion criteria and including several recently published studies, confirms Shapleske *et al*'s finding of decreased asymmetry of the planum temporale in schizophrenia.

Crow *et al* (1989) reported that the temporal horn of the lateral ventricle was larger in the right hemisphere in the normal control group of their post-mortem study, probably owing to the more extended language-related cortex at the dominant side. The present results from the meta-analysis on healthy subjects confirm this finding. However, while Crow reported reduced asymmetry of the temporal horn in schizophrenia, the present meta-analysis found no significantly decreased asymmetry in schizophrenia.

Asymmetry of the superior temporal gyrus is also frequently used as an indication of language lateralisation (Pearlson *et al*, 1997; Highley *et al*, 1999; Holinger *et al*, 1999; Levitan *et al*, 1999). However, direction and magnitude of asymmetry of this structure is not well established in healthy subjects. In this meta-analysis, controls showed a trend towards asymmetry favouring the right hemisphere, while the superior temporal gyrus was found to be greater on the right in patients. The trend towards rightward asymmetry in healthy subjects is surprising since it partly overlaps with Wernicke's area. However, the superior temporal gyrus also incorporates primary and secondary auditory cortex that generally shows rightward asymmetry, reflecting right hemispheric dominance for non-verbal sounds (Zattore *et al*, 1992). The posterior segment of the superior temporal gyrus might be a better candidate to reflect cerebral dominance for language, since it mainly consists of language-related heteromodal cortex (Pearlson, 1997). However, in the current meta-analysis, this segment also showed a trend towards asymmetry favouring the right hemisphere in healthy subjects. Therefore, neither the superior temporal gyrus, nor its posterior segment appears suited for the assessment of cerebral dominance for language.

Limitations

The presented paper included only studies on language lateralisation that used the dichotic listening paradigm. We were unable to retrieve enough visual half-field studies using language stimuli to allow for meta-analysis. Data of functional imaging studies are considered to be too diverse regarding technical assessment and statistical analysis to allow for direct comparison in a meta-analysis (Lange, 1999). A second limitation of the study is our choice to include only studies on patients with strict diagnosis of

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schizophrenia, excluding studies that used the broad DSM–II criteria for schizophrenia and studies that used patients with schizophrenia-spectrum disorders. Another reason that several studies could not be included was the absence of healthy control groups. By applying these strict inclusion criteria, the total number of studies was lower, but the contrast between the experimental and the comparison group was maximal.

Clinical implications

The reported excess of non-right-handedness and decreased right-ear advantage in healthy relatives of patients with schizophrenia suggest a genetic cause underlying the decreased cerebral lateralisation in schizophrenia. If this were true, a deviation of the genetic mechanism underlying cerebral dominance, the hypothesised 'right-shift factor' may cause a vulnerability to schizophrenia (Annett, 1999; Crow, 1999). This implies that the search for genes predisposing for schizophrenia may focus on loci that have a role in the establishment of cerebral dominance. In addition, indicators of decreased cerebral dominance in individuals, such as non-right-handedness, decreased right-ear advantage on the dichotic listening paradigm or decreased asymmetry of the planum temporale may help to identify subjects at increased risk for schizophrenia.

In sum, when literature on handedness, dichotic listening studies and asymmetry of language-related structures is reviewed quantitatively, compelling evidence emerged for decreased cerebral dominance in schizophrenia.

CLINICAL IMPLICATIONS

- Finding the locus of the gene for cerebral dominance may unravel the genetic predisposition for schizophrenia.
- Mixed- and left-handed subjects may be at increased risk of schizophrenia.
- The dichotic listening paradigm or measurement of planum temporale asymmetry may help identify subjects at increased risk of schizophrenia.

LIMITATIONS

- Visual half-field studies using language stimuli were not included.
- Functional imaging studies with language activation were not included.
- Narrow definitions were used for inclusion in the schizophrenia and healthy groups.

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