Behavioural relevance of atypical language lateralization in healthy subjects


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Summary

In most humans, language is lateralized to the left side of the brain. It has been speculated that this hemispheric specialization is a prerequisite for the full realization of linguistic potential. Using standardized questionnaires and performance measures, we attempted to determine if there are behavioural correlates of atypical, i.e. right-hemispheric and bilateral, language lateralization. The side and degree of language lateralization were determined by measuring the hemispheric perfusion differences by functional transcranial Doppler ultrasonography during a word generation task in healthy volunteers. Subjects with left (n = 264), bilateral (n = 31) or right (n = 31) hemisphere language representation did not differ significantly with respect to mastery of foreign languages, academic achievement, artistic talents, verbal fluency or (as assessed in a representative subgroup) in intelligence or speed of linguistic processing. These findings suggest that atypical hemispheric specialization for language, i.e. right-hemisphere or bilateral specialization, is not associated with major impairments of linguistic faculties in otherwise healthy subjects.

Keywords: functional Doppler ultrasonography; language lateralization; neuroscience; hemispheric dominance; behaviour

Abbreviations: CBFV = cerebral blood flow velocity; fTCD = functional transcranial Doppler sonography; MCA = middle cerebral arteries

Introduction

Hemispheric specialization is epitomized by the frequent disruption of language after left-sided brain lesions. Although the reason for this specialization is unknown, it is often assumed that the functional lateralization of the human brain has an adaptive value and may even present a prerequisite for the full realization of the linguistic potential (Luria, 1973; Geschwind and Galaburda, 1985; Hiscock, 1998). It has been speculated that functional neuronal clustering in one hemisphere during language development allows faster linguistic processing because transition times are shorter than in transhemispheric operations (Kupferman, 1995; Miller, 1996). Thus, gradually developing lateralization in children has been proposed as an explanation of why susceptibility to aphasia after unihemispheric lesions seems to increase with advancing age and language capabilities (Lenneberg, 1967; Vargha-Khadem et al., 1991). Disturbances in the development of lateralization have even been linked to the pathogenesis of dyslexia (Orton, 1937; Lenneberg, 1967; Annett et al., 1996). In a recent study of relative hand skills, Crow and colleagues reported deficits in a number of intellectual measures in subjects at the point of ‘hemispheric indecision’, i.e. in subjects who had equal skills in both hands on checking an array of squares on a printed sheet (Crow et al., 1998). Others have advertised ‘enhanced lateralization’ techniques for the treatment of dyslexia, attempting to force children to use their left hemisphere (van den Honert, 1977).

The theoretical simplicity of the hypothesis that language lateralization conveys an evolutionary advantage is intriguing. But there is little empirical evidence to support this view other than observations of brain-damaged patients with atypical lateralization. In these patients, however, dysfunction of language results from the lesion itself, and atypical lateralization is often a secondary, reorganizational phenomenon (Vargha-Khadem et al., 1985).

Assessment of language lateralization is now possible by various non-invasive functional imaging techniques which allow non-invasive studies in large groups of subjects without brain damage. Functional transcranial Doppler sonography (fTCD) measures changes in event-related cerebral perfusion...
that are related to neuronal activation in a way comparable with functional MRI (Deppe et al. 2000a). Because fTCD integrates and averages repeated activations within the whole territory of the insonated middle cerebral arteries, it provides a reliable measure of the hemispheric lateralization of language (Knecht et al., 1996, 1998a, 2000a, b; Deppe et al., 1997).

In the present study, we attempted to clarify the behavioural relevance of hemispheric specialization in a cohort of subjects without developmental or other known medical disturbances who had been examined previously for language lateralization by fTCD (Deppe et al., 1997). Using standardized questionnaires, we looked for correlations of the hemispheric lateralization of perfusion during word generation with measured by dual transcranial Doppler ultrasonography of the downstream increase in cerebral blood flow velocity (CBFV) in the basal arteries, as an indicator of the downstream increase in regional metabolic activity during the language task, were measured by dual transcranial Doppler ultrasonography of the middle cerebral arteries (MCAs). Ultrasonography was performed with two 2-MHz transducer probes attached to a headband and placed at the temporal windows of the skull bilaterally. After automated rejection of artefacts, data were integrated over the corresponding cardiac cycles, segmented into epochs that related to the cueing tone, and then averaged. The epochs were set to begin 15 s before and to end 35 s after the cueing tone. The mean velocity in the 15-s precueing interval ($V_{\text{pre.mean}}$) was taken as the baseline value. The relative CBFV changes ($dV$) during cerebral activation were calculated using the formula:

$$dV = (V(t) - V_{\text{pre.mean}}) \times 100/V_{\text{pre.mean}}$$

where $V(t)$ is the CBFV over time. Relative CBFV changes from repeated presentations of letters (on the average 20 runs) were averaged time-locked to the cueing tone.

An fTCD laterality index $LI$ was calculated using the formula:

$$LI = \frac{1}{t_{\text{int}}} \int_{t_{\text{int}}}^{t_{\text{int}}+5s} \Delta V(t) dt$$

where $\Delta V(t) = dV(t)_{\text{left}} - dV(t)_{\text{right}}$ is the difference between the relative velocity changes of the left and right MCAs. The term $t_{\text{max}}$ represents the latency of the absolute maximum of $\Delta V(t)$ during an interval of 10–18 s after cueing, i.e. during verbal processing. For integration, a time period of $t_{\text{int}} = 2$ s was chosen. The test–retest reproducibility of this procedure (Pearson product moment correlation coefficient) was $r = 0.95$, $P < 0.0001$ (Knecht et al., 1998b).

Goodness of recording
To control for goodness of the Doppler sonographic recording, the root mean square of the averaged CBFV fluctuations in the control condition ($-17$ to $-3$ s before the cueing tone) was calculated. All recordings with root mean square values greater than 2% of the averaged CBFV were discarded. This applied to ~1% of recordings.

Categorization of language representation
Left-hemisphere language dominance was assumed in all cases in which there was a positive $LI$ that deviated by

Methods
The study was part of the Münster functional imaging project on the variability of hemispheric specialization in health and disease (Deppe et al., 1997, 2000b; Knecht et al., 1998a, b, 2000a, b). The project involves the building of a growing database on functional cerebral lateralization in healthy subjects.

Inclusion and exclusion criteria for subjects and patterns of language lateralization with respect to gender and handedness have been reported before (Knecht et al., 2000a, b). Briefly, healthy volunteers were recruited by newspaper advertisement. The advertisement especially invited subjects who were not right-handed to participate. Subjects were not reimbursed. Subjects were excluded if information obtained from a standardized questionnaire suggested neurological disorders, particularly perinatal asphyxia or kernicterus, head trauma, loss of consciousness, epileptic seizures, meningitis or encephalitis, or delayed or disturbed language development. Subjects were also excluded if they had failed to complete the equivalent of a high school qualification (‘Realschul–Abschluss’ or ‘Abitur’). Additionally, $\sim 3\%$ of the subjects were excluded because fTCD could not be performed because of inadequate sonographic penetration of the skull. Another 1% of subjects were excluded from further analysis because the standards set for goodness of recording were not met (see below). A total of 326 subjects were finally included in the study; 198 were female (age range 15–49 years, mean 26 years, SD 5.1 years) and 128 were male (age range 19–46 years, mean age 26 years, SD 4.6 years).

Determination of language lateralization
The details of fTCD and the distribution of language lateralization in the cohort under study have been reported in detail in a preceding paper (Knecht et al., 2000b). Here we only describe details of the technique that are relevant for the quantification of language lateralization and are critical issues for this study. fTCD has been validated by direct comparison with intracarotid amobarbital injection and functional MRI (Knecht et al., 1996, 1998a, b; Deppe et al., 1997, 1998). Briefly, subjects silently generated as many words as possible, starting with a particular letter displayed on a computer monitor. Task compliance was monitored by having subjects report the words after a second auditory signal, 15 s after presentation of the letter. After a relaxation period of 60 s, the next letter was presented in the same manner.
Atypical language lateralization

>2 SE from 0. Right-hemisphere language dominance was assessed in a similar way. In cases in which LI did not deviate by >2 SE from 0, lateralization was classified as ‘low’. To ensure that noisy recordings would not produce false categorization as low, the criterion of goodness of recording was introduced. Because the lack of lateralization could not be explained by a lack of cooperation, which had been controlled for, low lateralization was considered to indicate bihemispheric language representation.

**Performance measures**

The average number of words per letter produced in the word generation task during the fTCD assessment was calculated as a direct index of verbal fluency. Verbal fluency is assumed to reflect the ease and quantity of verbal production and is related to the level of education (Ratcliff et al., 1998). Additional performance measurements were assessed in a subgroup of the cohort (n = 21) selected to represent the whole spectrum from left to right language lateralization (Figs 5 and 6). This group was recruited by categorizing all subjects as having left, bilateral or right language dominance according to the criteria outlined above. From each group, the seven subjects who had been examined last and were available for additional testing were subjected to IQ testing with the Hamburg Wechsler Intelligence Test for Adults, i.e. the complete form of the German version of the Wechsler Adult Intelligence Scale (Hamburger–Wechsler Intelligenztest für Erwachsene Revision 1991; Tewes, 1991).

To obtain a measure of linguistic processing speed, we had subjects perform a picture–word verification task (Fig. 1). Thirty black-and-white drawings of concrete objects were shown on a computer screen for 1.5 s each. They were taken from the repertoire of drawings standardized for name agreement and visual complexity by Snodgrass and Vanderwart (Snodgrass and Vanderwart, 1980) and depicted well-known objects such as animals and tools. Because each drawing was shown once with a correct and once with an incorrect subtitle, there was a total of 60 pictures in each block. Pictures were presented in a randomized order. Drawings

**Standardized questionnaires**

Handedness was assessed with the Edinburgh Handedness Inventory (Oldfield, 1971), in which scores range from −100 for strong left-handedness to +100 for strong right-handedness. For statistical analysis, handedness was grouped into the following categories: >75; 75 to −75; <=75.

A standardized questionnaire was used to screen subjects for the number of foreign languages spoken fluently. The number of languages was assumed to indicate linguistic talent. Academic achievement, i.e. a university qualification, was chosen as an additional indicator of linguistic proficiency (Tainturier et al., 1992). Furthermore, subjects were asked about artistic activities. They had to report whether they were actively involved in music, painting or sculpture. Such activities were taken to reflect artistic inclination and, by inference, artistic ability. Some authors perceive artistic ability as a faculty complementary to verbal ability and as being subtended by the right hemisphere (Peretz et al., 1997).

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**Fig. 1** Schematic of the measurement of linguistic processing speed. The mean accuracy and response times (RT) in a picture–word verification task and a motor control task were calculated and the values for the motor control task were subtracted from those for the picture–word verification task in order to obtain an index of linguistic processing speed. *(Maus* is German for mouse; *Löwe* is German for lion).*
measured approximately $15 \times 15\,\text{cm}$ and the subtitles were presented in 24-point Times Bold font. The distance between the subject and the computer monitor was standardized to 0.7 m. The screen was positioned at eye level. Subjects were instructed to press two buttons with both index fingers if the subtitles matched the picture and two different buttons with the two middle fingers if they did not. Each subject received eight practice blocks (with 60 trials each) at the beginning to overtrain reaction time performance (plateauing of reaction times). The fastest response of either hand was used for further analysis. Only correct picture–word verifications were included for the calculation of mean reaction times. As a motor control task, subjects were requested to respond as quickly as possible upon presentation of either a screen that was coloured red (button-press with both middle fingers) or green (button-press with both index fingers).

**Results**
The distribution of language lateralization was roughly bimodal, 264 subjects being left-hemispheric, 31 being low-lateralized and 31 being right-hemisphere dominant (Fig. 2).

**Standardized questionnaires**
As reported previously, a correlation was observed between handedness and lateralization of language, right dominance being more common in left-handed subjects than in right-handers (Deppe et al., 1997). No other behavioural measure was related to language lateralization (Table 1). Also, the three handedness groups did not differ in the numbers who engaged in artistic activity or had received university training, or in the number of languages spoken. Results for single measures are displayed in Figs 3–5.

**Performance measures**
No correlation was found between the average number of words produced during the word generation task and language lateralization ($r = 0.02, P = 0.69$) or the degree of handedness ($r = 0.11, P = 0.04$) (Fig. 6). In the selected group ($n = 21$), the overall IQ did not correlate with language lateralization ($r = 0.1, P = 0.65$) (Fig. 7), nor was there a significant relationship with verbal IQ ($r = 0.004, P = 0.9$) or performance IQ ($r = 0.05, P = 0.8$).

In the picture–word verification task, subjects did not differ from each other with respect to the numbers of correct and false responses. No significant correlations emerged between language lateralization and motor or linguistic processing speed, as measured by response times during the motor and linguistic tasks (Fig. 8). Response times in the picture–word verification task did correlate negatively with IQ ($r = -0.55, P = 0.009$), i.e. the higher the IQ, the faster subjects were in picture–word verification.

**Discussion**
In a group of 326 healthy subjects, no statistically significant differences in the number of foreign languages spoken fluently, academic achievement, participation in artistic activities, IQ, verbal fluency or speed of linguistic processing

<table>
<thead>
<tr>
<th>Table 1 Language lateralization and behavioural measures</th>
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<tbody>
<tr>
<td>Lateralization by fTCD (mean ± SD) Left 3.48 ± 1.50 Low 0.1 ± 1.18 Right -3.58 ± 1.88</td>
</tr>
<tr>
<td>Sample size (n) 264 31 31</td>
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<tr>
<td>No. of languages (median) 3 3 2</td>
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<tr>
<td>University qualification (n) 189/264 22/31 21/31</td>
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<tr>
<td>Artistic ability (n) 187/264 23/31 26/31</td>
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<td>Statistics Kruskal–Wallis $H = 2.2, P = 0.3$</td>
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<tr>
<td>$\chi^2(2) = 0.1; P = 0.9$</td>
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<td>$\chi^2(2) = 2.22; P = 0.3$</td>
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were found between individuals with left-hemisphere, bilateral or right-hemisphere language representation during word generation.

**Methodology**

Our study was designed to detect functional impairments associated with anomalous language lateralization in subjects who were otherwise normal and healthy. We specifically wanted to exclude subjects with pathological hemispheric specialization. Therefore, our subjects had to have an unremarkable medical history and meet minimal scholastic standards. This reduced the behavioural variability in our cohort but was necessary to minimize the possibility of covert brain lesions. (Of course, behavioural measures or imaging techniques can never fully exclude covert lesion.) Despite these conservative inclusion criteria, sample size was sufficient in each group (i.e. groups with left- and right-hemisphere and bilateral language processing) for statistical comparison.

We did not evaluate language lateralization against the ‘gold standard’, the intracarotid amobarbital procedure (Wada, 1949). Rather, we measured language task-related increases in blood flow. The intracarotid amobarbital procedure involves brain inactivation, whereas techniques sensitive to blood flow involve brain activation. However, a close correlation between the two approaches has been shown in several studies in healthy subjects and neurological patients with typical left-hemisphere and atypical right-hemisphere language lateralization (Desmond et al., 1995; Binder et al., 1996; Knecht et al., 1997; Rihs et al., 1999).

Our analysis was conceived in the tradition of lateralization research and was designed to detect hemispheric perfusion differences rather than bilaterality. However, because language lateralization during word generation was found to occur along a continuum from left to right dominance, we were faced with a subgroup of subjects with low or absent lateralization, although there was good cooperation during the language task and adequate recording (Fig. 2). This suggested that, in individuals with low lateralization indices, both hemispheres were involved in word generation.

While the distinction between left and right language dominance is mathematically self-evident, the definition of

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**Fig. 3** Lack of a systematic relationship between language lateralization and the number of foreign languages spoken fluently (Kruskal–Wallis test; $H = 2.2, P = 0.3$).

**Fig. 4** Lack of a systematic relationship between language lateralization and academic achievement [$\chi^2(2) = 0.19, P = 0.9$].

**Fig. 5** Lack of a systematic relationship between language lateralization and participation in artistic activities [$\chi^2(2) = 2.22, P = 0.3$].
Bilaterality of language is artificial and depends on the method employed to classify lateralization. Bilateral language representation would not become evident in stroke patients because bihemispheric insults impair consciousness and are fatal in most cases. The definition of bilaterality of language varies considerably in the published work using the intracarotid amobarbital procedure. Bihemispheric or ambilateral language representation is frequently reported during the disruption of neural function by the intracarotid amobarbital procedure in candidates for resective epilepsy surgery because of brain pathology. Rasmussen and colleagues reported that 19% and Risse and colleagues reported that 20% of non-right-handed patients had bilateral speech representation (Rasmussen and Milner, 1977; Risse et al., 1997). Benbadis and colleagues reported evidence for speech representation in both hemispheres in 12% of patients (Benbadis et al., 1995). Additionally, several lines of evidence indicate that even in otherwise typical people some components of language reside in the subdominant hemisphere (Bottini et al., 1994; Demonet et al., 1994; Boatman et al., 1998; Buchinger et al., 2000). We opted to define conservatively a group of subjects with ‘low lateralization’ when the lateralization index was close to zero, i.e. it did not deviate from zero by more than two standard errors of the averaged perfusion differences. A total of 9% of our subjects (biased for left-handers) fell into this group. A recent fMRI study focusing on the Broca region roughly corroborates this finding, reporting ‘bilateral’ activation in 14% of 100 healthy subjects during word generation (Pujol et al., 1999).

**Atypical lateralization**

Non-left-hemisphere language dominance and non-right-handedness have time and again been associated with atypical behaviour, be it good or bad. Inspired by the reportedly ambidextrous Leonardo da Vinci and Michelangelo, it has been suggested, for example, that bilaterality is associated with superior cognitive and creative skills (Mebert and Michel, 1980; O’Boyle and Benbow, 1990). Others hold the opposite view. Atypical cerebral dominance is taken as an indicator of behavioural disturbance because the reverse is true, i.e. abnormal lateralization is frequent in brain-damaged patients with behavioural impairments (Coren and Halpern, 1991). Additionally, there is a general tendency to associate atypical lateralization with behavioural impediments simply because the statistical norm is assumed to represent the biological optimum. It has therefore been proposed that cerebral functional lateralization is a necessity for the full realization of linguistic and cognitive potential (Luria, 1973; Geschwind and Galaburda, 1985; Hiscock, 1998). According to this hypothesis, transcallosal conduction delay would make multiple passes during language processing prohibitively slow (Ringo et al., 1994). Although deviating from the statistical norm of left-hemisphere language dominance, right-hemisphere language dominance as a mirror organization of left-lateralization does not challenge the conceptual
framework of lateralization as a precondition for higher cognitive functions. Bilateral language representation, however, does pose a challenge. Crow and colleagues have taken handedness as a correlate of cerebral dominance and, using a sample of >12000 individuals, have demonstrated global deficits in subjects with low indices of handedness as well as in subjects with extreme right-handedness (Crow et al., 1998). They interpret their finding as reflecting the operation of continuing selection on a gene involved in language lateralization. In large population studies it is difficult to exclude covert brain damage, particularly when no stringent exclusion criteria have been established. Thus, behavioural impairments and pathological non-right-handedness can both be sequels of brain injury (Dellatolas et al., 1993). Other studies of healthy subjects were unable to prove that non-right-handedness conveys any selective disadvantage over right-handedness other than a possibly increased predisposition to accidents in left-handers who need to deal with tools and equipment designed for the safety and convenience of right-handers (Salive et al., 1993; Coren and Previc, 1996).

Our study was based on a smaller sample but one with more stringent exclusion criteria than the sample studied by Crow and colleagues. Crow and co-workers excluded from their population the bottom 10% in terms of square ticking ability to examine whether their results had been influenced by a sub-group in whom hand skill in general was impaired. After doing so, they still found deficits at the point of equal hand skill (Crow et al., 1998). More importantly still, we were able to evaluate hemispheric language dominance directly. Our data did not demonstrate that atypical, particularly bilateral, language representation is associated with any behavioural cost or peculiarity. Moreover, there was no behaviourally relevant slowing of language processing in subjects with bilateral language representation. Such a slowing would have been predicted by the hypothesis that language needs to be processed in a lateralized fashion because transcallosal operations are prohibitively slow (Ringo et al., 1994). We addressed this issue specifically by measuring linguistic processing time in a picture–word verification task corrected for variability in motor responses (Fig. 1). This task was sufficiently sensitive to detect differences in response times in subjects differing in IQ, which have long been known in the psychological literature (Sommers et al., 1970). The role of conduction delay is further questioned by a recent finding in a patient with agenesis of the corpus callosum, i.e. with a transcallosal conduction stop, who had no speech impairment and had bilateral language representation, as indicated by PET and the Wada test (Komaba et al., 1998). Rather than a transcallosal delay, transcallosal inhibition could have a role in the development of lateralization. Transcallosal inhibition is a characteristic of the adult brain but does not develop fully before 5 years of age (Heinen et al., 1998). It appears to play a role in the coordination of independent limb movements. One may speculate that subjects with bihemispheric language representation are those in whom bilateral brain regions were dedicated to language before transcallosal regions became effective.

**Limitations of the study**

This study cannot exclude that there is a behavioural relevance of atypical language lateralization. The number and type of behavioural aspects we could assess were limited. Because the focus of the study was language lateralization, academic attainments and behavioural measures were chosen which relate, although in some cases only indirectly, to linguistic aptitude, i.e. the number of foreign languages spoken fluently, academic achievement, IQ, verbal fluency and speed of linguistic processing. Some of these qualities (skill in foreign languages and academic achievement) could only be assessed by subjective reports. More detailed and controlled measurements (IQ and speed of linguistic processing) were possible only in a subgroup of subjects reflecting the spectrum from left- to right-hemisphere language dominance. We therefore cannot exclude positively the possibility that there are more subtle linguistic or other behavioural correlates of language lateralization. For example, we did not follow subjects to determine whether there is an increased risk of schizophrenia in those with atypical language lateralization, as has been suggested by Crow (Crow, 1997).

**Conclusion**

Our study provides strong evidence that atypical hemispheric language lateralization results in no major behavioural anomaly. Comparable linguistic proficiency can apparently be achieved despite considerable variation in the underlying neural system.

Like others, we are still inclined to believe that the prevailing pattern of left-hemisphere language dominance, like right-handedness, is not a random phenomenon but has been influenced directly or indirectly by evolutionary selection. For example, it is feasible that an adaptive advantage of left-lateralized neural—linguistic or non-linguistic—processing during the evolution of the human brain may have been minimal or even undetectable at the level of the individual. Only through amplification by repetition over thousands of generations could this advantage have led to a trend for lateralization of language. At present, however, there may be one paradoxical consequence of language lateralization. With today’s increased life expectancy and the increased likelihood of suffering a unihemispheric ischaemic stroke, subjects with bilateral language representation may be less likely to become aphasic or, at least, may recover better from language disturbances compared with people with strong lateralization. A possible disadvantage in the evolutionary past might thus have become an advantage today.
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