Epileptic activity influences the speech organization in medial temporal lobe epilepsy

J. Janszky,1,2 H. Jokeit,1 D. Heinemann,1 R. Schulz,1 F. G. Woermann1 and A. Ebner1

1Epilepsy Center Bethel, Bielefeld, Germany and 2Epilepsy Center, National Institute of Psychiatry and Neurology, Budapest, Hungary

Summary
Factors influencing atypical speech lateralization have theoretical importance in understanding the organization and reorganization of higher cognitive functions, as well as having practical implications, especially in brain surgery and neurorehabilitation. Atypical (right-sided or bilateral) language representation is more frequent in focal epilepsy than in healthy people. This difference is thought to be related to early childhood brain injuries localized in the neighbourhood of speech centres. The effect of epileptic activity on speech lateralization has not been investigated, although much data suggest that epileptic activity may interfere with higher brain functions. It can only be evaluated in a homogeneous human population with epilepsy having the same lesion type in the same localization. For these reasons, we investigated 184 patients with medial temporal lobe epilepsy (MTLE) due to unilateral hippocampal sclerosis (HS), but without other epileptogenic lesions. All patients underwent comprehensive presurgical evaluation. In MTLE, the influence of age at the time of brain damage, i.e. the initial precipitating injury (IPI), could be evaluated separately from the other timing factors. Of 100 patients in whom a Wada test was performed, left-sided speech occurred in 76% of the left-sided and in 100% of the right-sided MTLE patients (P < 0.05). For further evaluation, we included only the 83 left-sided MTLE patients. The mean age at seizure onset was 10.1 ± 7.8 years (range 1–37 years); the mean age at evaluation was 35.7 ± 9.8 years. Based on the Wada test, left-sided speech was present in 63 patients, while in 20 (24%) patients the Wada test revealed atypical speech dominance. We found that atypical speech representation in left MTLE was associated with higher spiking frequency (P < 0.05) and with sensory auras representing an ictal involvement of the lateral temporal structures (P < 0.01). Psychic auras suggesting limbic seizure spread showed a significant association with left-sided speech dominance in left MTLE (P < 0.05). Neither age at epilepsy onset, nor age at IPI was associated with atypical speech in left MTLE. Conclusively, we found that in patients with focal epilepsy, not only the known factors, i.e. the age at which the brain injury occurred and its localization, but also the epileptic activity itself, i.e. interictal discharges and seizure spread, may influence speech reorganization. Our findings also suggest that not only structural elements but also functional factors have an effect on the language organization of the brain.

Keywords: language reorganization; mesial temporal lobe epilepsy; interictal epileptiform discharges; seizure spread

Abbreviations: fMRI = functional MRI; HS = hippocampal sclerosis; IEDs = interictal epileptiform discharges; IPI = initial precipitating injury; MTLE = medial temporal lobe epilepsy

Introduction
Factors influencing typical and atypical speech lateralization have received a great deal of attention because they have theoretical importance in understanding the organization and reorganization of higher cognitive functions, as well as practical implications, especially in brain surgery and neurorehabilitation. In patients with epilepsy, speech lateralization is more frequently atypical in comparison with healthy people (Springer et al., 1999). This is not surprising because in many patients the cause of focal epilepsy is a morphological abnormality which frequently is developmental or acquired in early childhood at an age when neuronal plasticity allows speech reorganization (Hecaen, 1976; Rasmussen and Milner, 1977; Springer et al., 1999). Such a brain abnormality may interfere with the normal neuroanatomical organization of cognitive functions resulting in reorganization, even if this abnormality is far from the.

Brain 126 © Guarantors of Brain 2003; all rights reserved
speech centres or does not affect the cortex at all (Staudt et al., 2001).

The presurgical evaluation prior to epilepsy surgery is comprised of a careful delineation of the epileptogenic lesion and the seizure onset zone. Moreover, it encompasses a comprehensive neuropsychological assessment including a Wada test, by which speech dominance can be determined (Ebner, 2001; Rosenow and Lüders, 2001). In the past years, many studies investigated speech lateralization in epilepsy patients (Rasmussen and Milner, 1977; Rausch and Walsh, 1984; Woods et al., 1988; Rey et al., 1988; Duchowny et al., 1996; Helmstaedter et al., 1997; Springer et al., 1999; Brazdil et al., 2002). These studies provide evidence that early injuries and lesions residing in the speech centres induce atypical speech lateralization, which is often associated with left-handedness. In pre-school children, injury affecting the left hemisphere results in an interhemispheric reconstitution of language functions to the right hemisphere (Hecaen, 1976; Rasmussen and Milner, 1977). After age 5 years when language becomes gradually lateralized (Kimura, 1967), contralateral language reorganization after brain injury occurs less frequently (Springer et al., 1999). The drawbacks of all these studies is that they included a mixed population of epileptic patients and not a circumscribed epilepsy syndrome. Consequently, in such populations, the different types of disturbances cannot be investigated adequately and separated from each other, i.e. the influence of age, localization, lateralization of the lesion and the epileptic activity itself.

Although some memory disturbances caused by epilepsy can be modelled experimentally in animals (Kotłoski et al., 2002), it is impossible to investigate speech in experimental models, as language is a unique human ability, the main basis for communication, human thinking and self-consciousness (Serafetinides et al., 1965; Popper and Eccles, 1977; Ebner et al., 1995). In this study, we investigated patients with medial temporal lobe epilepsy (MTLE) who exclusively had hippocampal sclerosis (HS), but no other epileptogenic lesion. In MTLE with HS, the seizure onset region is localized to the mesiotemporal structures (Williamson et al., 1993); thus, it is a unique, homogeneous epilepsy syndrome (Engel et al., 1998). Moreover, it is the most frequent chronic focal epilepsy. Human and experimental data suggest that the cause of HS is thought to be due to an initial precipitating injury (IPI) occurring in early childhood or infancy, which induces functional and structural damage to the hippocampus gradually evolving to HS (Maher et al., 1995; Mathern et al., 1995, 2002; Toth et al., 1998; Chen et al., 1999; Dube et al., 2000; Schulz and Ebner, 2001). The factors that influence speech reorganization can be investigated in MTLE since these patients have the same pathology in the same location, and this pathology is located distantly from the eloquent speech areas. The influence of the timing of the brain damage (i.e. IPI) can also be evaluated separately from the other timing factors, e.g. onset of non-febrile seizures. In addition, the influence of epileptic activity can be investigated independently from the lesional factors.

The present study addressed whether timing factors, gender, lateralization or the epileptic activity are responsible for the evolution of atypical speech. The novelty of our study has been that by evaluating a homogeneous epilepsy population, we were able to investigate the effect of epileptic activity on speech organization separately from the lesion effects. To our knowledge, except for the epilepsy onset, no other study has investigated the epileptic factors in speech organization.

**Methods**

**Patients**

In this retrospective study, we included 184 adult patients (85 men and 99 women, aged 19–59; mean: 35.2 years) who consecutively underwent presurgical evaluation at our centre from 1994 to 2002 and had intractable MTLE associated with HS. There were 102 patients with left-sided and 82 patients with right-sided MTLE. One hundred and twenty-five patients had epilepsy surgery with >1-year follow-up; 74% of them became seizure free postoperatively.

Our further inclusion criteria were: (i) complex partial seizures proved by ictal video-EEG which are characteristic of MTLE; (ii) definitive interictal epileptiform discharges (IEDs, spikes or sharp waves) above one or both temporal regions; patients with extratemporal or generalized IEDs were excluded; and (iii) unilateral hippocampal sclerosis detected by high-resolution MRI. We defined HS if both hippocampal atrophy and increased T2 signal intensity in hippocampus were present on MRI. Patients with bilateral HS or any other abnormalities other than HS (e.g. dual pathology) were excluded. The examinations were made exclusively on 1.5 or 1.0 T Siemens Magnetom MR machines. Sagittal T1, axial T2 as well as coronal T1, T2 and proton density or FLAIR (fluid attenuated inversion recovery) sequences perpendicular to the long axis of the hippocampus were made, which gave adequate delineation of the temporal lobes.

**Clinical history**

The data regarding the age at the first unprovoked seizure, usual seizure frequency, presence of generalized tonic–clonic seizures, presence and type of aura, and the timing of the IPI thought to be the original cause for HS were derived from medical records. At admission to the presurgical unit, all patients and (if available) their parents were asked about the history of the IPI and other epilepsy risk factors.

**Clinical examinations**

All patients underwent an internal, neurological, psychiatric and neuropsychological examination at admission to our in-patient department. For evaluation of handedness, the Edinburgh Inventory was used.
Non-invasive continuous video-EEG monitoring
All patients underwent continuous video-EEG monitoring lasting 3–7 days as a part of their presurgical evaluation. EEG recordings with 32–64 channels were used; electrodes were placed according to the 10–10 system. In most cases, sphenoidal electrodes were also used. Interictal EEG samples were automatically recorded and stored by computer. In this study, the first 2 min of each hour stored automatically by the computer were evaluated. The location and frequency of IEDs as well as the EEG seizure localization were analysed.

Wada test procedure
The Wada test was necessary for presurgical evaluation of memory and language functions in 100 patients, 17 of whom had right-sided MTLE. Our Wada test procedure has been described elsewhere (Jokeit et al., 1997). Immediately after the injection of amobarbital into the arteria carotis interna, the patient was asked to perform simple verbal tasks and non-verbal actions followed by naming objects, pictures, numbers and colours, as well as reading words and sentences in order to test speech functions of the investigated hemisphere. Speech lateralization was based on semi-quantitative evaluation of a patient’s performance in expressive and receptive language tasks during the Wada test. Initial speech arrest and, later on, word-finding problems, paraphasias, global aphasia, fluent aphasia and non-fluent aphasia describe frequent disturbances of language. Up to 5 points were given for complex language tasks depending on the severity of the language disturbance: 0 = no reaction; 1 = not understandable; recurring utterances; 2 = spontaneous and incorrect repetition; neologisms, paraphasias; 3 = spontaneous incorrect and correct repetition; 4 = correct self-correction; 5 = unimpaired. Simple tasks such as ‘Show me your tongue’ were credited with 1 point because they merely test speech reception. The maximum number of points amounted to 104, reflecting complete unimpaired speech production of the investigated hemisphere.

Investigated variables and statistical methods
The following timing factors were chosen: age at the Wada test, duration and onset of epilepsy, age at the IPI. We also investigated the lateralization and localization of the epileptic activity characterized by the following variables: seizure frequency, presence of secondarily generalized seizures, spike frequency, presence of interictal and ictal bilateral epileptic activity, as well as different aura types. The latter were chosen because they suggest a limbic, temporolateral or other seizure propagation. All variables were chosen according to whether they were previously reported in influencing speech lateralization or because it was reasonable to assume that they may have an effect on this process.

For the multivariate analysis of variables which were supposed to be associated with atypical speech representation, a stepwise logistic regression was performed. For bivariate analysis, Mann–Whitney U test was used for continuous and Fisher’s exact test for categorical variables. Two-tailed error probabilities smaller than \( P < 0.05 \) were considered to be significant.

Results
Of 100 patients in whom the Wada test was performed, left-sided speech occurred in 75.9% of the left-sided and in 100% of the right-sided MTLE patients (\( P < 0.05 \)). Thus, no patients with right-sided TLE had atypical speech lateralization. Atypical speech lateralization was correlated with left-handedness: 10 of 20 patients (50%) with atypical speech were left-handed, while of 80 patients with left-sided speech, left-handedness was present in seven cases (9%, \( P < 0.001 \)).

For the Wada test, there was a strong bias for the left-sided patients (see Methods). This bias was because in the presurgical evaluation of MTLE, the main indication for the Wada test is memory testing and not the investigation of speech lateralization. Left-sided MTLE patients are known to have a much higher risk for disabling postoperative memory loss than right-sided MTLE patients (Jokeit et al., 1997; Gleissner et al., 1998; Rausch et al., 1998). Due to this bias, for the further evaluation, we included only those 83 patients in whom an amobarbital (Wada) test was performed, and those who had a left-sided MTLE in order to identify factors responsible for atypical speech lateralization.

Of 83 left-sided MTLE patients having taken the Wada test, there were 36 men and 47 women. The mean age at seizure onset was 10.1 ± 7.8 (range 1–37) years, the mean age was 35.6 ± 9.8 (range 19–59) years. Ten patients had a family history of epilepsy. An IPI which may lead to HS was present in 51 patients (61%): febrile seizures in 34; cerebral infections in 11; significant cerebral trauma in six; and perinatal asphyxia in two patients. All IPIs occurred before age 7 years. There were 67 right-handed and 16 non-right-handed (ambidextrous or left-handed) patients. Based on the Wada test, left-sided speech was present in 63 patients, while in 20 patients the Wada test revealed atypical (right-sided or bilateral) speech dominance. None of the patients had a neurological deficit. Of 83 patients, 62 patients had epilepsy surgery with >1-year follow-up; 73% of them became seizure free postoperatively (category I according to Engel).

We compared patients with left-sided versus atypical speech according to general data, clinical history, interictal and ictal epileptic activity. A stepwise forward logistic regression was performed except for age at IPI and spike frequency.

Table 1 shows the general data and the clinical history of patients with or without left-sided speech. No variables showed significant differences in the two groups. Because all IPIs occurred before age 7 years and only five of them appeared after age 3 years, we did not categorize the age at IPI according to pre-school age because in all but one patient the IPI occurred before pre-school age. Inclusion of
categories of ages at the IPI in the logistic regression model would have reduced the number of patients to 51 because IPIs were present in only 61% of the cases. Of patients in whom a history of IPI was evident, 38 had left-sided speech, while 13 had atypical speech. Patients with left-sided speech had an IPI at the mean age of 20 ± 18.7 months, while those who had atypical speech had an IPI at the mean age of 13 ± 9.6 months, but this difference was not significant according to the Mann-Whitney test. We also performed a Fisher’s exact test to determine whether age at IPI before 1 year was associated more often with atypical speech. In patients in whom an IPI occurred before age 1 years, atypical speech occurred in 31%, while left-sided speech was present in 69% of the patients. Conversely, in patients in whom an IPI occurred after age 1 years, atypical speech was present in 21%, while left-sided speech was present in 79% of patients; the difference between the two groups was not statistically significant.

Table 2 presents the laterality of interictal and ictal epileptic activity and aura characteristics of patients. Investigating the severity of interictal epileptiform activity, we examined only patients with unitemporal spikes because patients with bilateral epileptiform activity and with frequent spikes might have an antagonistic effect on speech lateralization if we suppose that epileptic activity may really influence speech lateralization. We found an association between the frequency of interictal activity in unilateral MTLE and atypical speech representation (P < 0.05, Mann-Whitney test). Patients with left-sided speech had a median spike frequency of 15.5 IEDs/h (25–75%, range: 2.25–80.5 IEDs/h), while patients with atypical speech had a median spike frequency of 48 IEDs/h (25–75%, range: 23.5–64 IEDs/h).

The presence of sensory auras (auditory, vertigous, somatosensory) suggesting a temporo-latero-posterior ictal spread was also associated with atypical speech, while psychic auras indicating a medial (temporo-limbic) seizure spread were significantly associated with typical speech lateralization (see Table 2).

Discussion

The main findings of our study are: (i) atypical speech dominance was only present in left-sided MTLE; (ii) 24% of patients with left MTLE had an atypical pattern of speech dominance; (iii) atypical speech representation in left MTLE was associated with higher spiking frequency and with sensory auras representing an ictal involvement of the posterior-lateral temporal structures (Ebner, 1994; Wunderlich et al., 2000); (iv) psychic auras suggesting a limbic seizure spread showed a significant association with left-sided speech
dominance in left MTLE; and (v) neither age at IPI, age at epilepsy onset nor gender was associated with atypical speech representation in left MTLE.

One of the major limitations of this study was that it was retrospective, thus, we could investigate epileptic variables, e.g. the severity of the interictal activity and the seizure spread as a variable at the time of Wada test, and not longitudinally or before the speech organization/reorganization evolved.

**Plasticity of language lateralization**

Both the executive speech region (Broca’s area) (Foundas et al., 1996) and perceptive secondary auditory centres (planum temporale) (Geschwind and Levitsky, 1968) show a morphological asymmetry in comparison with the contralateral homologous brain regions in favour of the left side. This asymmetry is already present in the last gestational trimester (Wada et al., 1975) and shows no change with increasing age, suggesting that the left–right functional differentiation follows a structural asymmetry that is already ‘pre-set’ (Geschwind and Levitsky, 1968). Human non-speech sounds, e.g. baby babbling (Holowka and Petitto, 2002) or non-verbal vocalizations in frontal lobe seizures (Janszky et al., 2000), may also be related to the left hemisphere, suggesting that not only speech, but vocalization at a subverbal level independent of age is also a product of the left hemisphere in humans. Moreover, the lateralization of sound production is not a human-specific phenomenon; subhuman vertebrates appear to have left hemisphere dominance of vocal productions (Walker, 1980). Others suggest that the left–right functional asymmetry is already present in the pre-language age in babies, i.e. the left hemisphere is specialized in the temporal modality of a given stimulus, while the right hemisphere is specialized in the spatial modality, which difference is the functional basis as to why language becomes confined to the left hemisphere (Witelson, 1987). Indeed, Dehaene-Lambertz et al. (2002) found that precursors of adult cortical language areas are already active in infants well before the onset of speech production. They investigated 3-month-old infants by using functional MRI (fMRI) activated by speech perception. They found that the left-lateralized brain regions similar to those of adults, including the superior temporal and angular gyri, were already active in infants during speech perception.

Despite this strong left-sided predisposition of the brain morphology and function, Chiron et al. (1997) suggested that the right hemisphere until age 3 years is still the dominant hemisphere considering the Broca and Broca-homologous areas, sensorimotor cortex and the temporoposterior regions. After age 3 years, a shift towards the left hemispheric dominance begins (Rasmussen and Milner, 1977; Marcotte and Morere, 1990) and may be completed at age 4–8 years (Hecaen, 1976; Rasmussen and Milner, 1977; Ameli, 1980; Vargha-Kadem et al., 1997; Balsamo et al., 2002). However, Gaillard et al. (2000) found that even children aged 8–12 years showed significantly more right hemispheric participation in speech production than adults. A recent fMRI study found that although there is a negative correlation between age at brain injury and speech reorganization, there is no cut-off point after which contralateral speech reorganization does not occur in epilepsy patients (Springer et al., 1999). Moreover, even in adult patients suffering from aphasia, Wada tests suggested that improvement of aphasia was paralleled by the participation of the right hemisphere in speech production, indicating some kind of contralateral speech reorganization in adulthood (Czopf, 1972).

**Effects of gender, lateralization and age at brain injury on speech representation**

There are contradictory data as to whether speech lateralization is related to gender. Some studies found that women had less frequent or weaker lateralized speech (McGone, 1977; Helmstaedter et al., 1997; Kansaku et al., 2000), whereas others found no sex difference in speech lateralization (Kertész and Sheppard, 1981) either in healthy subjects (Frost et al., 1999; Knecht et al., 2000) or in epilepsy patients (Springer et al., 1999). We also found no difference in gender for speech lateralization.

Although most studies found that left-sided lesions may cause contralateral speech reorganization (Rasmussen and Milner, 1977; Rausch and Walsh, 1984; Rey et al., 1988; Woods et al., 1988; Helmstaedter et al., 1997), a recent fMRI study did not find such a correlation (Springer et al., 1999). However, this study did not include left-handed patients, and the number of patients was relatively small. In our study, we found that atypical speech dominance was present in only left-sided MTLE, whereas atypical speech did not occur in right-sided MTLE, which confirms a recent study investigating temporal lobe epilepsy (Brazdil et al., 2002).

It may be questioned by which mechanism a lesion localized to the mesiotemporal region can influence the speech lateralization when this lesion is rather far from the eloquent speech centres and no morphological abnormalities in the speech centres were visualized by high-resolution MRI. Even left periventricular white matter lesions acquired perinatally may be associated with atypical speech lateralization (Staudt et al., 2001), thus it is possible that an IPI leading to hippocampal damage is able to cause a left–right shift of the language organization. Surprisingly, in our study, neither the age at the presumed brain injury, i.e. the IPI, nor the age at epilepsy onset was correlated with atypical speech representation in left MTLE. These findings may be a result of a bias for the age at IPI and development of HS in early childhood (Sagar and Öxbury, 1987; Schulz and Ebner, 2001). Indeed, in our study, most IPIs occur before age 3 years, and only one patient had an IPI after pre-school age, i.e. almost all known IPIs of our patients occurred at an age when the brain plasticity certainly allows a left–right shift of speech centres. Thus, the age effect of brain injury is not pronounced.
in MTLE because all brain injuries occurred at the age of maximal brain plasticity. The question is why all the patients did not have a right–left speech shift due to the early brain injury; in other words, which factors induce or do not induce speech reorganization after an early brain injury affecting the left side.

Effects of seizures and interictal epileptiform activity on speech lateralization

Similarly to Springer et al. (1999), we did not find a cut-off age at seizure onset after which no atypical speech can occur. Moreover, the participation and the reorganization capacity of the right hemisphere for speech functions is present to some degree even in adolescence or adulthood (Czopf, 1972; Gaillard et al., 2000). Thus it is reasonable to assume that not only the timing of the first seizures, but other epileptogenic factors as well may participate in speech reorganization in epilepsy.

Previous studies investigating the speech reorganization in epilepsy did not consider the ictal or interictal epileptological data. In this study, we hypothesized that not only the lateralization and localization of the injury and age, but also the functional disturbance caused by epileptic activity may also play a role in the organization of speech in epilepsy. This could be answered in our study because (i) all patients had left-sided brain injury and epilepsy; (ii) all patients had the same pathology in the same localization; (iii) no patient had a lesion in the brain regions responsible for the speech production; and (iv) the age at the brain injury (IPI) was not correlated with atypical language because most patients probably had an early brain injury.

Experimentally evoked repeated seizures induce a long-term spatial memory deficit in rats (Kotloski et al., 2002). Few data concerning human epilepsy suggest that temporal lobe seizures had short-term and probably also long-term effects on human memory functions (Jokeit et al., 2001). Not only the memory, but even speech lateralization may be directly influenced by temporal lobe seizures. Jayakar et al. (2002) reported a case of a 14-year-old child in whom, after a cluster of left temporal lobe seizures, the language-activated fMRI using four different tasks suggested a right temporal receptive speech centre. Two weeks later, when the patient had their usual seizure frequency, the fMRI using the same tasks was repeated and revealed a left temporal receptive speech centre. Dominant temporal lobe seizures cause ictal and post-ictal speech disturbances in 75% of patients (Gabr et al., 1989), suggesting that they can disturb speech production, at least transiently. PET studies suggest that seizures cause not only transient, but also sustained functional disturbance (Savic et al., 1997; Schlaug et al., 1997). Consequently, it is reasonable to assume that frequent ictal involvement of lateral temporal structures may occasionally result in long-term functional speech disturbance which may induce a more prominent participation of the contralateral structures in speech production, finally resulting in a reorganization of speech.

In MTLE patients, the seizures originating in mesiotemporal regions can spread to the ipsilateral (lateral) temporal neocortex and to the limbic structures without involving the lateral temporal regions, or they may show an initial frontal, mainly fronto-orbital spread (Lieb et al., 1991; Gloor et al., 1993), without involving the frontal speech centres.

We found that seizure spread had an influence on the speech organization in epilepsy. Namely, sensory auras typically representing a tempo-posterior seizure involvement (Ebner, 1994; Wunderlich et al., 2000) were associated with atypical speech in left MTLE, indicating that seizures may cause a long-term functional disturbance in the left auditory/speech receptive region and may induce contralateral speech reorganization. On the other hand, seizure spread probably not involving the lateral neocortical regions (complex partial seizures with psychic auras) was associated with left-sided speech.

Not only the seizures, but also the interictal epileptiform activity may disturb higher cognitive functions, potentially leading to functional reorganization. Frequent interictal epileptiform discharges may result in transient cognitive impairment, while such impairment is absent in those periods when no interictal epileptiform activity occurs, e.g. during neuropsychological testing (Aarts et al., 1984). Moreover, an impairment of spatial task performance was demonstrated during right-sided interictal discharges, while during left-sided paroxysm, the verbal cognitive performance was disturbed (Aarts et al., 1984). This suggests that the cognitive impairment caused by interictal spikes is not non-specific, but reflects the functional disturbance in the area where the spikes originate or to which they are propagated. Consequently, we can assume that frequent interictal activity propagating to the speech centres may also cause speech disturbances.

Spikes in MTLE are generated in the mesiotemporal structures. Conversely, 10–50% of them propagate to the lateral temporal neocortex (Niedermeyer and Rocca, 1972; Alarcon et al., 1994; Clemens et al., 2003). Since we did not use intracranial electrodes in this study, the spike frequency was related to the degree of the interictal epileptic involvement of the temporal neocortex. In this study, we found that the higher spike frequency was associated with atypical speech. Thus, our findings may indicate that even the interictal epileptic activity may interfere with the functions of the temporal speech receptive areas.

Our study was retrospective; thus, we do not know when the transfer of speech occurred. Therefore, it is also not completely clear whether it was progressive during the course of the epilepsy due to the interictal and ictal epileptic activity, as we suppose considering our results, or earlier, as a mere consequence of the IPI that caused the epilepsy and determined by the extent of brain damage caused by the IPI, independent of the age of its occurrence. Our data could stimulate prospective and longitudinal studies in children and
adolescents, using non-invasive methods for determination of speech dominance (for instance fMRI or fTCD), prospectively, from early in the course of MTLE.

Conclusion
We found that in patients with focal epilepsy, not only the known factors, i.e. the age at and the localization of the brain injury, but also the epileptic activity itself, interictal and ictal activity, could be responsible for speech reorganization. Our findings also suggest that the question of whether an early prevention of the development of epilepsy after a known IPI should be reconsidered. Because in patients with left-sided brain injury, even if the speech centres had shifted to the right hemisphere ‘escaping’ from the seriously damaged functions, poor verbal cognitive performance was found (Helmstaedter et al., 1997), this suggests that the speech reorganization (i.e. the replacement of language functions from the predetermined regions) does not mean a complete restitution of speech functions. Our findings also suggest that not only structural elements but also the functional factors may have an effect on the language organization of the brain.

Acknowledgements
We wish to thank Terri Shore Ebner who carefully reviewed the manuscript as a native English speaker. This work was supported by a grant from the Deutsche Forschungsgemeinschaft (DFG-Eb 111/2-2 to A.E.) and Humboldt Stiftung (to J.J.).

References


Received February 27, 2003.
Revised April 11, 2003. Accepted April 16, 2003