

Language processing in aphasia: changes in lateralization patterns during recovery reflect cerebral plasticity in adults

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Abstract

During single word processing the negative cortical DC-potential reveals a left frontal preponderance in normal right-handers as well as in patients with a history of transient aphasia. Lateralization of DC-negativity therefore provides a reliable and robust method for the assessment of language dominance. In 11 stroke patients with permanent aphasia this physiological pattern changed to bilateral activation reflecting an additional right-hemispheric involvement in compensatory mechanisms in aphasia. Along with complete clinical recovery the classical aphasic syndromes revealed specific differences in changes of their lateralization patterns. In Broca's aphasia the initial right-hemispheric preponderance changed to a left frontal lateralization while in Wernicke's aphasia a presumably permanent shift towards the right hemisphere occurred. Differences in lateralization patterns might reflect different mechanisms of recovery such as the initial disinhibition of homologous areas contralaterally and subsequent collateral sprouting and synaptic modulation. The assessment of changes in lateralization of the cortical DC-potential during language tasks is a non-invasive, safe method with excellent time resolution that might provide further insights in the neural basis of recovery from aphasia. © 1997 Elsevier Science Ireland Ltd. All rights reserved

Keywords: Slow cortical potentials; Aphasia; Cortical plasticity; Cerebral dominance; Language processing

1. Introduction

It is a longstanding clinical observation, that language functions recovered after left-hemispheric stroke are abolished if the patient suffers an additional right-hemispheric lesion (Cambier et al., 1983; Lee et al., 1984; Basso et al., 1989). These clinical experiences suggest a language processing capacity of the right hemisphere, a hypothesis that gained additional support by split brain investigators (Gazzaniga, 1983) and lesion studies (Gorelick and Ross, 1987; Ross et al., 1988).

Although the right hemisphere (RH) under physiological conditions seems to be rather limited in purely linguistic language processing (see Joannette et al., 1990 for review), several investigations support the clinical observations of right-hemispheric involvement in recovery from aphasia due to a left-hemispheric lesion (Moore, 1984; Papanicolaou et al., 1987). In particular, cerebral blood

flow (CBF) studies by Xenon-CT-Scans (Knopman et al., 1984a) suggested an increase in the right inferior frontal region in patients with incomplete recovery from aphasia. Additional evidence for a right-hemispheric involvement in the residual language of aphasic stroke patients with left-hemispheric lesions comes from the intra-carotid injection of barbiturates into the RH. This resulted in severe deterioration of residual language (Kinsbourne, 1971; Czopf, 1979). At rest, positron emission tomography (PET) revealed consistent metabolic abnormalities in the left temporo-parietal region in all aphasic patients, but no correlations were detected between aphasia scores and the metabolic measures of the right hemisphere (Karbe et al., 1990; Metter et al., 1990). Recently, a PET-study of fully recovered aphasic patients performing a verb generation task showed a right-hemispheric activation in the superior temporal gyrus as well as an increased left frontal activity (Weiller et al., 1995).

The assessment of shifts of the cortical DC-potential during cognitive tasks provides several advantages in comparison to the aforementioned methods. Recorded from the scalp, this is a non-invasive method which therefore can be

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used repeatedly with normal volunteers and patients for longitudinal studies. The high temporal resolution at the expense of a lower spatial resolution is another advantage for correlative investigations. The neurophysiological basis of this method is the post-synaptic depolarization and thereby activation of larger populations of cortical neurons that leads to local changes of the cortical DC-potential. DC-potential shifts during mental activity therefore allow the determination of brain areas involved in specific cognitive processes, i.e. motor preparation (Lang et al., 1988), memory (Rösler et al., 1993), and visual motion perception (Patzwahl et al., 1994). During a language processing task a left-hemispheric lateralization over the frontocentral region was found in 93% of right-handers (Altenmüller et al., 1993) and 65% of left-handers (Altenmüller, 1989). In patients with known cerebral dominance an excellent correlation with the lateralization of DC-shifts during the search for synonyms could be demonstrated (Altenmüller et al., 1993). The determination of the language dominant hemisphere by the assessment of DC-potential shifts during language processing was demonstrated (Altenmüller et al., 1993) to be as specific as the Amytal test (Rasmussen and Milner, 1977) or as electroconvulsive shocks (Warrington and Pratt, 1973).

The purpose of the present study was to evaluate a possible role of the undamaged RH in acute and recuperant aphasia due to left-hemispheric stroke. This was done by use of cortical DC-potential distribution monitoring during language processing.

2. Subjects and methods

2.1. Subjects

Eleven right-handed patients and a control group of 12 normal volunteers were tested. All normal volunteers were evaluated a second time 1 month later with a different order of stimulus presentation to assess retest reliability. Patients and volunteers scored 100% right-handedness in the Edinburgh Handedness Inventory (Oldfield, 1977) and had a minimum of 12 years of education.

The patient group comprised 11 patients who had suffered a left-hemispheric stroke causing a permanent neurological deficit including one of the classical aphasic syndromes. 4 patients revealed typical Broca's aphasia, 4 suffered from anomia and 3 had a deficit predominantly in comprehension typical for Wernicke's aphasia. The CT-scans demonstrated ischemic or hemorrhagic lesions of the left hemisphere, mostly cortical and subcortical ($n = 5$) in location but also solely subcortical ($n = 4$) or cortical ($n = 2$).

Seven of these patients were studied in the acute phase of the stroke, between 2 and 4 weeks after the onset of symptoms. According to clinical experience the peracute, mostly cytotoxic, edema is resolved within 2 weeks (O'Brien, 1995). Possible extracellular edema due to a

disrupted blood-brain barrier, known to be longer-lasting (O'Brien et al., 1974), has been demonstrated to have remarkably little effect on electric activity and evoked responses (Sutton et al., 1980). The 4 other patients could not participate in experiments at this stage because of the severity of their aphasia and therefore were tested after clinical stabilization. Ten patients were studied twice at different points in their clinical course of recovery. None of our patients required an antiedematous treatment. The patients' medications were identical at both measurements and included long-term anti-hypertonic medication (betablocker) in 4 patients, anti-diabetic therapy (insulin) in two and an anti-convulsant (phenytoin) in one. All patients received acetylsalicylic acid (100–250 mg daily) for stroke prophylaxis. At the time of the first assessment all patients revealed a mild to moderate impairment in the performance of the Aachen Aphasia Test (AAT), a standardized neuropsychological test battery for the distinction of aphasic syndromes in the German language (see Huber et al., 1984 for description). When recovery from aphasia was clinically evident, a second evaluation was conducted. Recovery was validated by an improved task solution score, indicated by the amount of synonyms found by the individual patients.

The clinical and demographic data of these patients are summarized in Table 1. AAT-scores in naming and speech comprehension as well as token test results are noted in T-standardized scores, that allow for the differentiation in degrees of severity of impairment with respect to the aphasic syndrome. AATs were conducted 4 weeks after stroke.

2.2. Procedures

The subjects had to search for synonyms to orally presented nouns, e.g. common objects (like house, boat, balcony) or abstract expressions (reason, humor, benevolence). An acoustic signal at the beginning of each trial prompted the patient to fixate a point in his or her visual field in order to avoid artifacts caused by eye movements. After the fixation movement, a 3 s prestimulus period (baseline) was recorded before another tone signal indicated the beginning of the stimulus period during which the noun was presented acoustically within 2 s. Subsequently, subjects had to search mentally, without any vocalization or tongue movement, for as many synonyms as possible until a final tone signal indicated the end of the trial after 4 s. After each trial subjects orally communicated the synonyms found. A total of 120 trials were conducted.

2.3. Data acquisition and analysis

DC-potentials were recorded from the scalp by non-polarizable AgCl-electrodes with an electrode impedance of less than 3 k Ω . Stabilization of the electrode potential

and reduction of the skin potential was reached using the method for high quality DC-recordings described by Bauer et al. (1989). Electrode positioning was conducted according to the Jasper 10/20 system over frontal (F3/F4), central (C3/C4), temporal (T3/T4) and parietal (P3/P4) regions using unipolar leads with linked earlobe electrodes as a reference. Simultaneously, vertical and horizontal eye movements (VEOG resp. HEOG) as well as galvanic skin response (GSR), tongue movements and respiration were recorded for artifact control.

DC-amplifiers (Fa. Toennies, Freiburg, Germany) with externally triggered DC-compensation were used. During the experiment, all traces were monitored on a 16 channel ink writer (Nihon-Kohden 4317-FG) for artifact control. Only trials without eye or tongue movements, sweating artifacts or DC-drifts, and with a correct task solution (i.e. synonyms or semantically related expressions) were accepted for averaging.

A minimum of 30 trials without artifacts were required from each subject for averaging. Data normalization was obtained by equating the mean of the preperiod with zero. Mean amplitude values averaged from the 4 s task period

were compared to the baseline period averages (Fig. 1). As, during the stimulus period, DC-potentials are confounded with short-latency components evoked by acoustical encoding and orientation, the individual activation and lateralization patterns were deduced from the task period which represents cortical activation during pure mental processing. Lateralization was assessed by comparison of mean amplitude values of homologous electrode sites. Difference amplitude values were calculated by subtracting the mean amplitude values of homologous electrode sites, e.g. F3 – F4, to express the degree of lateralization. Individual performance was determined by calculating the percentage of correctly found synonyms of all trials finished (synonym score).

Mean values during the stimulus and the task period were subjected to statistical analysis by repeated measure analysis of variance (ANOVA) incorporating one group factor (control vs. patients) and 4 within-subjects factors: period (stimulus vs. task-period), recording (first or second) and hemisphere (left, right), and position (frontal, central, temporal, parietal). The mid-line electrodes were analyzed separately. In order to demonstrate changes in

Table 1
Clinical data on stroke patients

Pt.	Age (yrs)	Sex	Months after stroke		Type of aphasia	AAT-subtests (T-values)				Synonym score (%)		CT findings
			Test 1	Test 2		Token	Repetit.	Naming	Comp.	Test 1	Test 2	
LS	60	f	6	12	Broca	60	60	62	65	49.1	60.5	L frontotemp. ischemia
WW	30	m	1	24	Broca	69	58	75	72	52	68.1	L fronto-precentral ischemia
HH	67	m	2	6	Broca	70	60	60	78	78.4	88.2	L frontotemp. ischemia
EB	68	m	1		Broca	73	55	62	69	20.8		L precentral ischemia
EM	70	m	6	12	Anomic	69	58	61	70	8	28.2	L temp. hemorrhagic ischemia
RL	29	m	4	24	Anomic	69	66	60	70	43	54.8	L parieto-occipital hemorrhage
IZ	44	f	2	12	Anomic	80	80	65	80	66.6	91	L parieto-temp. ischemia
WU	49	m	1	24	Anomic	63	62	64	62	12.2	15	L capsular ischemia
EG	57	f	1	12	Wernicke	57	66	52	50	12.3	31	L parieto-occipital hemorrhage
IS	57	f	1	9	Wernicke	59	66	46	55	35.8	37.5	L temporo-parietal ischemia
AK	70	m	9	20	Wernicke	70	67	53	55	45	54.2	L parieto-occipital ischemia

Clinical and demographic data on 11 stroke patients revealing lesion type and location as well as severity of aphasia assessed by means of the Aachen Aphasia Test (AAT) using T-standardized values. Critical cut-off values are 62 for mild, 52 for moderate and 43 for severe impairment. The synonym score reflects individual performance (correctly found synonyms in percent of all trials finished). L, left.

distribution rather than amplitude, ANOVA was repeated with normalized data according to McCarthy and Wood (1985). For corrections of violations of the sphericity assumption the Huynh-Feldt epsilon was used.

3. Results

3.1. Normal subjects

Fig. 1 depicts the averages of a right-handed volunteer to exemplify our evaluation procedure. The course of the obtained average potential starts off with an evoked potential (N 100) at the beginning of the stimulus period with its maximum amplitude over Cz reflecting an orienting response to the first tone signal that indicated the acoustic presentation of a noun (Näätänen and Picton, 1987). The N

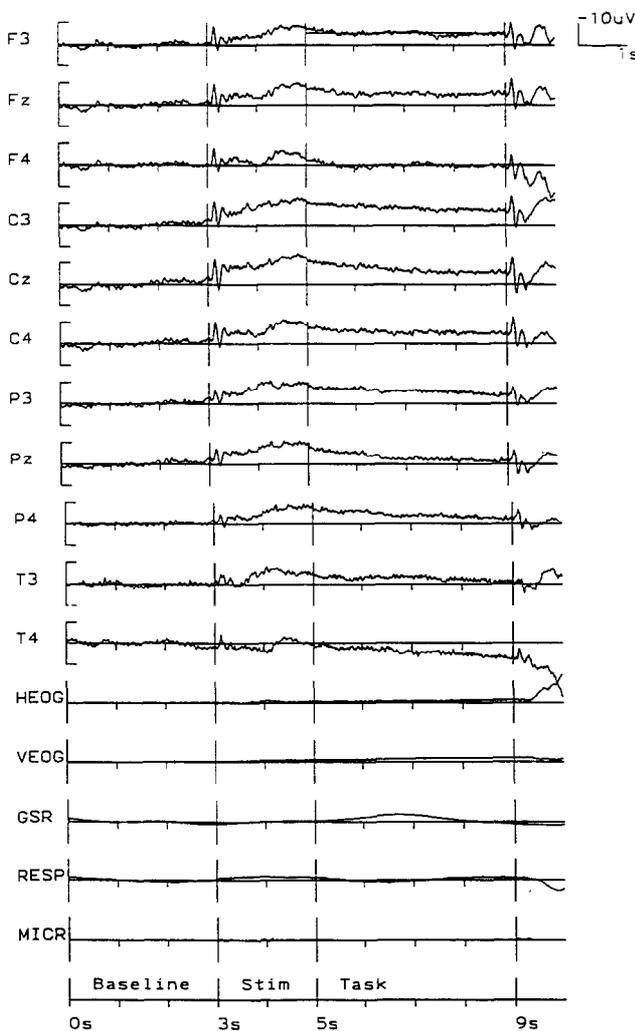


Fig. 1. Average of a healthy volunteer demonstrating the 3 different periods for evaluation: a 3 s preperiod, a 2 s stimulus period and a 4 s task period. The mean amplitude value of the task period compared to baseline is depicted in the uppermost recording. VEOG and HEOG as well as GSR and respiration were recorded for artifact control.

100 is followed by a large bilateral negativity of about 1 s which most likely reflects early acoustic processing of the stimulus as well as attentional activation (Näätänen, 1982; Uhl et al., 1990). The following sustained negative DC-potential shift during the 4 s task period occurs predominantly over left frontal, central and temporal regions with maximum amplitude over F3. The mean amplitude value of the 4 s task period is depicted by a horizontal line in the left frontal recording. Original data and inter-individual variances in amplitude are demonstrated in scatterplots (Fig. 2) that display the mean amplitudes over left versus right frontal, central, temporal and parietal brain regions. An increase in negativity occurs over the left hemisphere in all subjects, which is highest in the left frontal area. In all 12 control subjects mean amplitude values at F3 exceeded those at F4, revealing a strong lateralization of the DC-shift towards the left frontal region. This effect is equally pronounced over central and temporal regions but cannot be detected in the parietal area.

3.2. Replication in normal subjects

Fig. 3 pictures a grand average of DC-potentials over 12 volunteers. The solid line represents the first experiment; the dotted line delineates the results of the second testing. Both traces correlate over frontal and central regions, thereby confirming an excellent retest reliability in these electrode positions, whereas over temporal and parietal brain regions the variability between the two measurements was considerably higher.

The scatterplots (Fig. 4) illustrate the individual difference values obtained by subtraction of mean amplitudes during the 4 s task period at homologous sites. Difference values reflect the degree of lateralization at the specific region and therefore are a measure for language lateralization. The high correlation in frontal leads demonstrates the reproducible lateralization in each individual subject. In the frontal and central leads almost all values are located in the right upper quadrant of the graph. Thus, both measurements resulted in a left frontal and central lateralization pattern. In the parietal and temporal regions a different picture is found. The difference values reveal a greater distance from the diagonal, positivation occurs as well as a change in lateralization, and thus indicate a considerable intra-individual variation from one experiment to the next in the temporal and parietal area.

As expected, statistical analysis revealed no significant difference between the first and second measurements in normals. This was true for both stimulus and task-period ($P = 0.288$ and $P = 0.36$, respectively). Neither in normals ($P = 0.523$) nor in patients ($P = 0.334$) were the variances of the mean amplitudes found to be significantly different between the first and the second measurement. As expected, there were significant differences between the subjects' variances in all 4 measurements ($P < 0.01$ in normals and $P < 0.001$ in patients).

NORMAL SUBJECTS

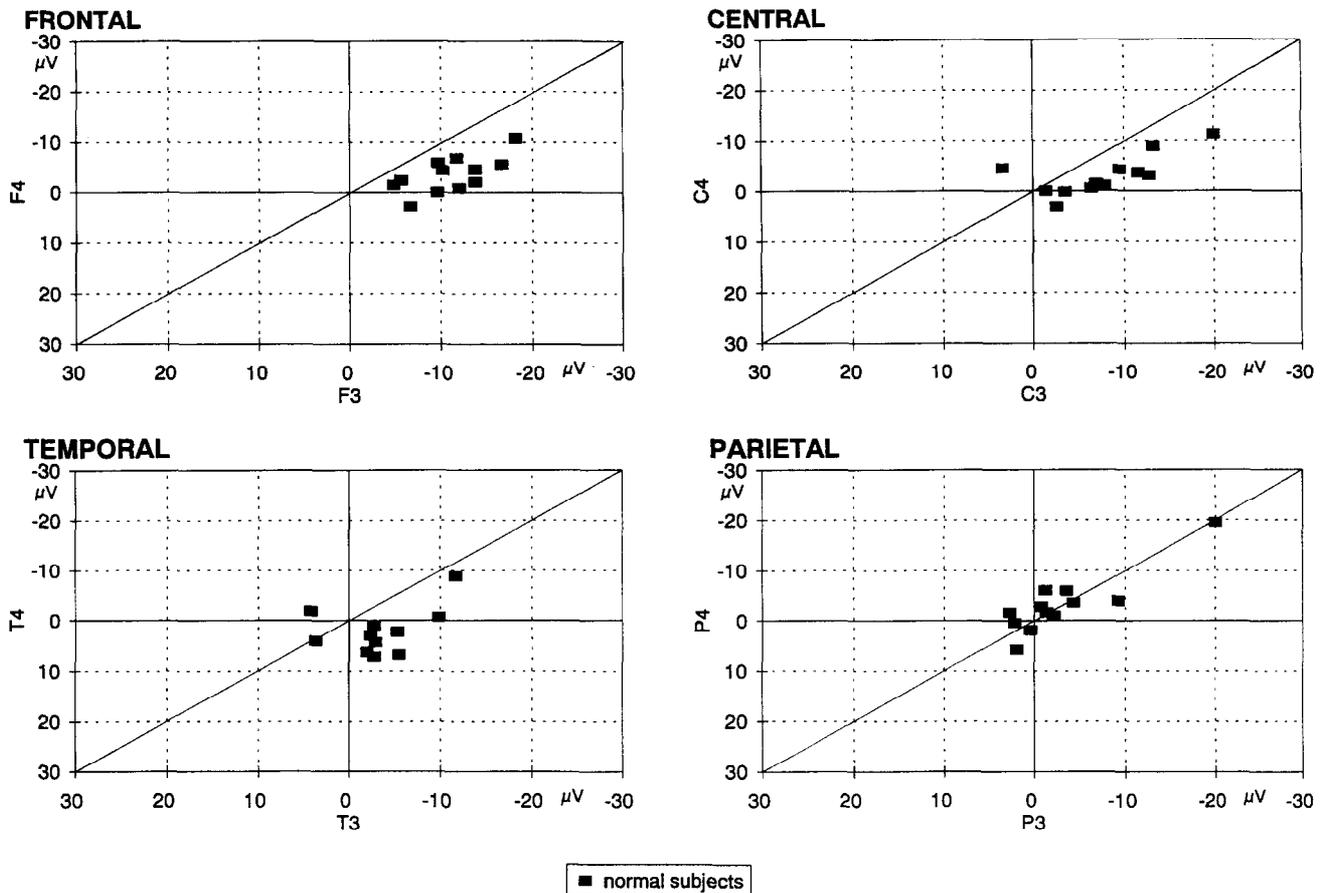


Fig. 2. Lateralization pattern in the control group. Mean averaged amplitude values in μV of frontal, central, temporal and parietal leads comparing the left (abscissa) and the right (ordinate) hemisphere. In the frontal area all subjects are represented below the diagonal, which illustrates a left frontal lateralization in 100% of subjects. Lateralization effects are less pronounced in central and temporal leads and absent in the parietal region.

3.3. Patients with aphasia

In comparison with our results obtained in normal subjects, the scatterplots presented in Fig. 5 reveal some remarkable differences. In the frontal and central leads no strong and systematic lateralization towards the left hemisphere as has been observed in normals (Fig. 2) can be detected in the group of aphasics taken as a whole. While Broca aphasics reveal a tendency to right-hemispheric preponderance, patients suffering from sensory aphasia of the Wernicke type show higher amplitudes over the left frontal region. In anomic aphasia no specific pattern can be observed. However, as the groups of the different aphasia types are small, the detected differences have to be interpreted with caution.

Statistical analysis revealed the following results. During stimulation period, there was no statistically significant difference between normals and patients ($P = 0.42$). During task period, significant differences occurred with

respect to the factor 'position'. In contrast to normals, patients showed larger negative shifts over right frontal and right central electrodes, corresponding to increased activation ($F4, P = 0.028$; $C4, P = 0.025$). When repeating ANOVA with normalized data, only the differences in the right central electrode position ($C4$) remained significant ($P = 0.04$), indicating an additional distribution effect with activation of brain regions located posterior to the BROCA-homologous region.

Differences between groups were also found with respect to the factor 'hemisphere', revealing a significantly different hemispheric distribution of electric activity during stimulus and task period in general ($P = 0.020$) and between groups ($P = 0.025$). Hemispheric lateralization patterns also proved to be significantly different between normals and patients ($P = 0.03$), confirming the lack of lateralization found in frontal regions in the patients. Due to the small number of patients, statistics could not be performed to test differences between the subgroups.

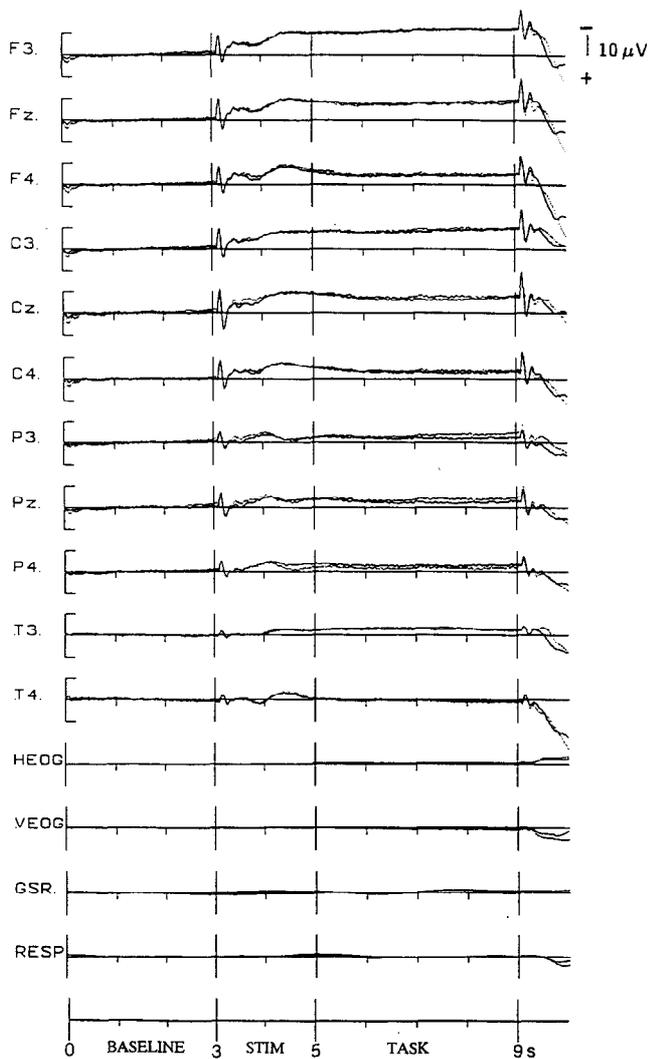


Fig. 3. Grand average over 12 normal subjects. The solid line represents the first measurement, the dotted line the second one. Both sets of averages are almost identical in shape and amplitudes.

3.4. Follow-up study in aphasics

The results of the follow-up study in stroke patients demonstrate various degrees of changes in the distribution of the negative cortical DC-potential that occur along with clinical recovery. An exemplary case of a patient with Broca's aphasia is shown in Fig. 6, demonstrating a shift of lateralization from the right to the left hemisphere along with clinical recovery. A change of hemispheric lateralization either from the left to the right side (right lower quadrant in Fig. 7) or from the right to the left hemisphere (left upper quadrant in Fig. 7) occurred in 4 patients in the frontal leads. In one patient with anomic aphasia the lateralization pattern changed from bilateral activation to a left-hemispheric preponderance.

Statistical analysis performed on the group of patients as a whole revealed significantly lower amplitudes in activation in the second measurement over right frontal

($P = 0.04$) and right central ($P = 0.01$) areas. When repeating ANOVA with normalized data, this decrease of negativation remained significant over the right central brain area ($P = 0.04$). A significant interaction of the factors 'measurement' and 'hemisphere' ($P = 0.037$) in the patients' group confirms the changes in lateralization patterns during recovery. A comparison of the data obtained in patients in the follow up measurements and the data obtained in controls during the second measurement showed no statistical difference, thus indicating the tendency of patients to regain a 'normal activation' pattern.

No correlation between time after stroke and lateralization pattern could be determined ($r < 0.5$ for all electrode positions). This may indicate a relationship of the type of aphasia or the state of recovery from aphasia to the pattern of lateralization rather than a pure correlation with time elapsed after stroke. Although the number of subjects in each aphasia group is small, specific trends in the type of change of cortical activation pattern during recovery can be detected. All patients with Broca's aphasia now demonstrate a left-hemispheric preponderance, illustrated by a location above the diagonal line in Fig. 7, two reveal a complete shift of laterality back towards the left hemisphere while one shows a more pronounced left-hemispheric lateralization after recovery. Two out of 3 patients with Wernicke's aphasia are located below the diagonal, thus indicating an increased activity of the right hemisphere. In anomic aphasia a tendency towards a leftward shift is observed, although one patient shows a change in lateralization to the right. The synonym score improved with recovery from aphasia from 40.1% to 52.8% (group mean), but no significant differences between the aphasia groups could be detected.

4. Discussion

4.1. Individual differences and uniformity of lateralization in normal subjects

Mental search for synonyms causes a bilaterally sustained negativity of the cortical DC-potential. The cortical distribution of this DC-shift exhibits a language-specific lateralization pattern most pronounced over the left frontal, central and temporal regions, while the parietal region reveals a smaller and more symmetrical negativity.

Several linguistic processes contribute to the production of synonyms to a given noun (Levelt, 1989). The acoustic stimulus has to be decoded and the phonological code is recognized as a word by the auditory lexicon. During the search for synonyms semantic associations are formed. The semantic lexicon comes up with ideas that are then articulatorily coded and stored in the working memory until the results of the search can be reported. According to results from electrocorticography (ECoG) by Ojemann et al. (1989), the neural activation caused by the described course of perceptive language processing can be recorded

REPLICATION

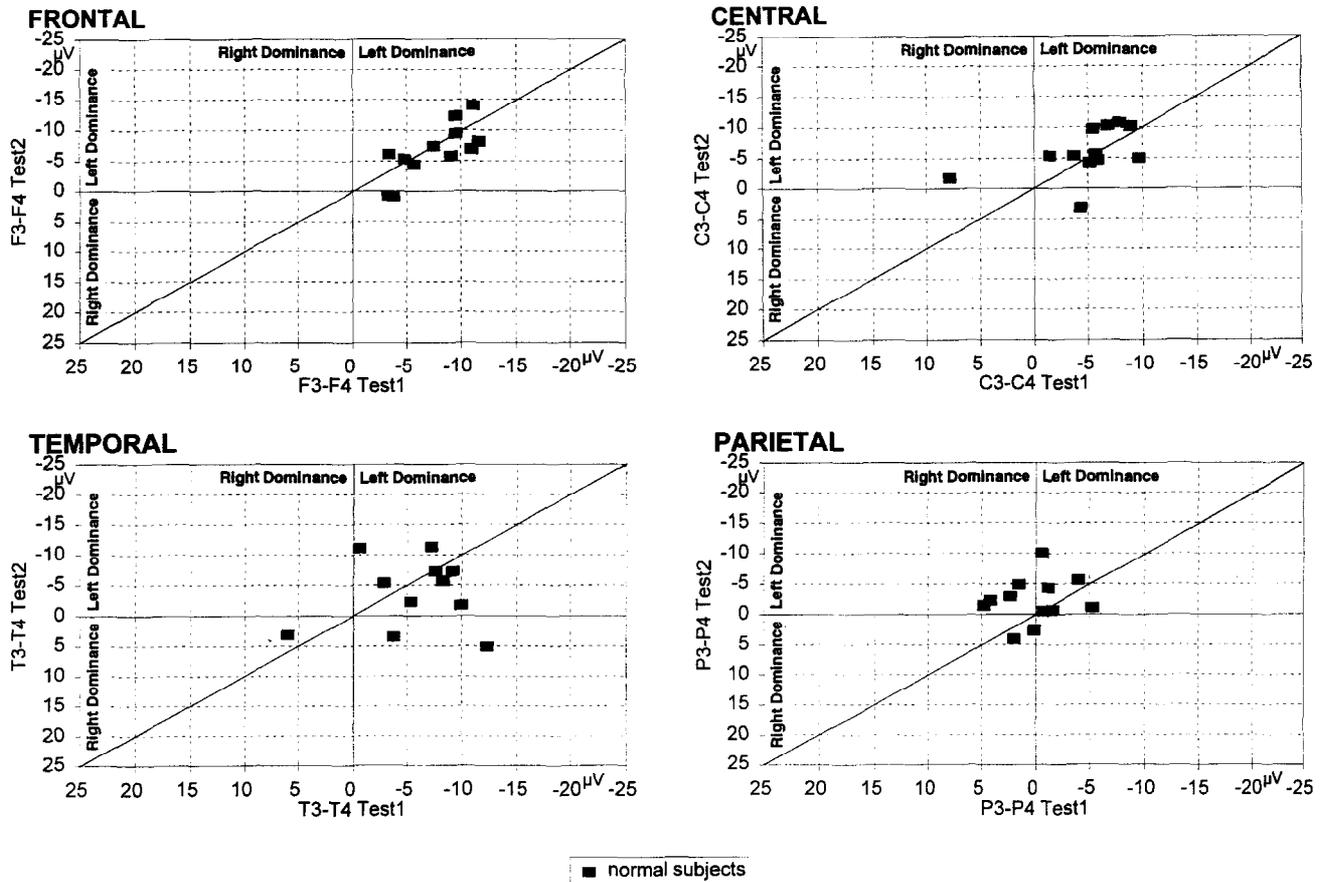


Fig. 4. Replication of lateralization patterns. Difference values (i.e. F3 – F4) obtained at the first measurement (abscissa) compared to the second measurement (ordinate) in frontal, central, parietal and temporal areas. Frontally, all dots apart from two are located close to the diagonal in the right upper quadrant indicating good replicability and a very robust lateralization pattern, while in temporoparietal regions considerable intra-individual variation occurs. Temporal value in one subject could not be calculated because of artifacts.

within 1 s. With our task the perceptive components of language processing therefore take place already during the stimulus period. Within the task period a continuous search for synonyms is performed in parallel with continuous storage of the findings in the working memory. In our opinion, the different language processes occurring during the task period converge on a continuously performed internal memorization of the synonyms found that requires internal speech mechanisms. Areas classically assigned to the motor preparation of speech like Broca's area have been shown to be activated also during the employment of inner speech mechanisms e.g. by generating verbs silently (Petersen et al., 1988; Petersen et al., 1989; Wise et al., 1991). Moreover, the supplementary motor area reveals an increase in rCBF not only in overt speech but also during silent verbalization (Petersen et al., 1989; Wise et al., 1991).

On the basis of the aforementioned findings the sus-

tained left frontal activation demonstrated by DC-potential shifts is most likely due to a language-specific, pre-motor activation. The language-related DC-negativity in the left frontal area can be clearly distinguished from a potential solely related to oral movements as it is highly lateralized and occurs without the actual performance of speech. In the temporal leads conspicuously smaller amplitudes were found compared to those in the frontal leads. The temporoparietal cortex, especially the superior temporal gyrus, according to PET-studies, is mainly involved in phonological decoding (Petersen et al., 1988) and lexical decision making (Frith et al., 1991). As these linguistic processes are not pertained for the whole 4 s period they might result in smaller amplitudes of the mean DC-potential over those electrodes.

Interindividual differences in amplitude size and in degree of lateralization are remarkable. Several factors account for those differences. Apart from individual phy-

APHASIC PATIENTS

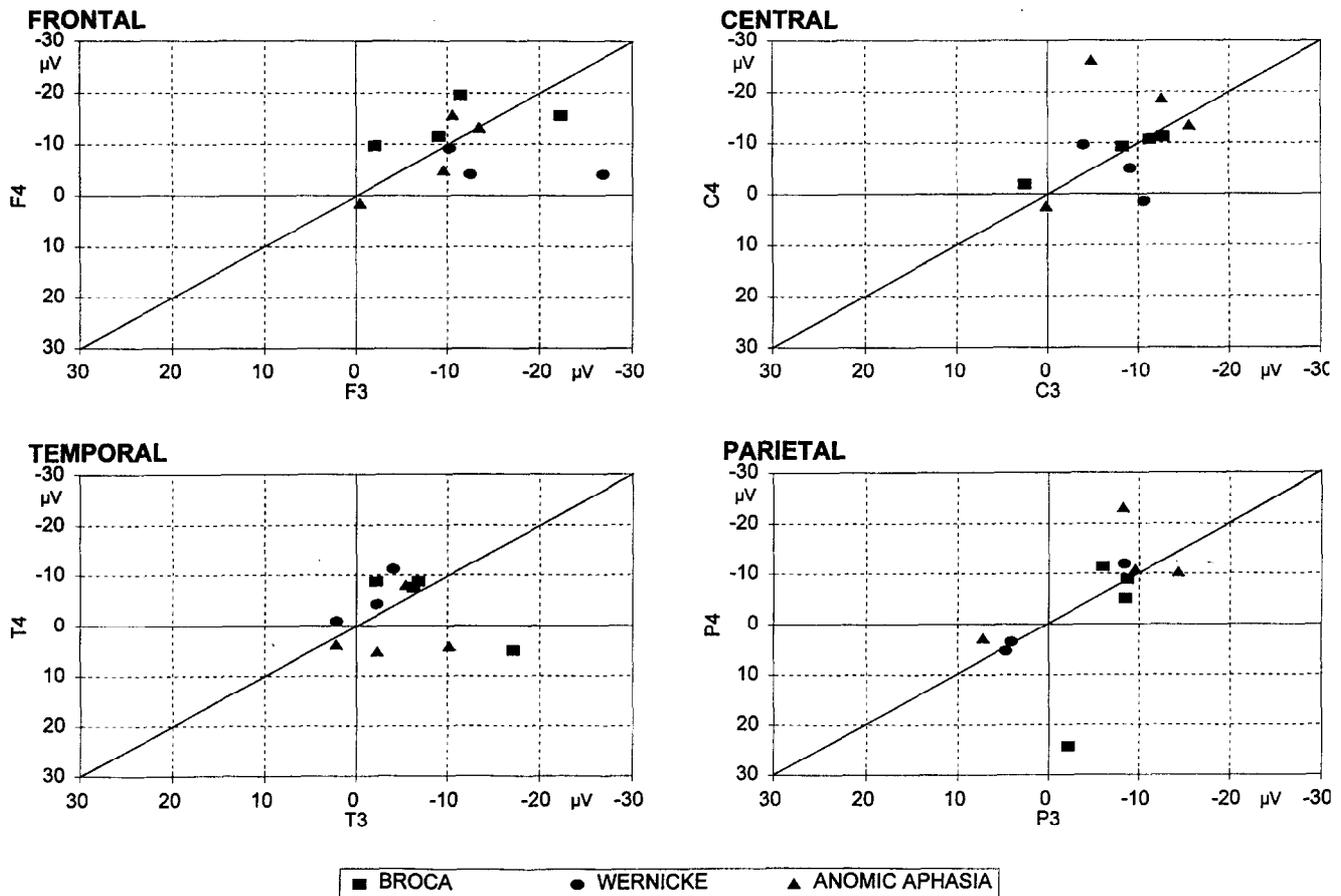


Fig. 5. Lateralization patterns in aphasia. In the group of aphasics taken as a whole the physiological frontal lateralization pattern towards the left cannot be detected. Rather, a preponderance of the right frontal region can be seen in Broca aphasics, while Wernicke patients exhibit the ordinary left frontal predominance. One Broca aphasic could only be tested in the acute phase but not during follow-up.

sical factors like scalp impedance (Lutzenberger et al., 1987), remarkable gross anatomical individual differences exist (Steinmetz and Seitz, 1991) and, moreover, functional language areas were found to be variable in location (Ojemann et al., 1989). Individual differences in verbal skills, arousal and attention might also have an impact on the subject's effort to solve the task (Rockstroh et al., 1989; Asenbaum et al., 1992).

Our replication data confirm an excellent retest reliability of the frontal left lateralization that again stresses the value of this robust measure of the individual's pattern of language lateralization. Electrical stimulation studies equally report no changes of the cortical pattern of language organization over time (Ojemann, 1991). Temporal and parietal activation patterns, in contrast, reveal intra-individual differences over time, which most likely reflect different strategies employed in the search for synonyms. Such search strategies comprise visualization involving

right temporo-parietal brain areas (Ely et al., 1989; Petsche et al., 1992) and verbal memory of the semantic and phonetic context of the given noun (Altenmüller et al., 1993).

The employment of other cognitive capabilities usable for a strategic search for synonyms and therefore helpful for verbal communication in general is at least one cause of the widespread and bilateral activation found in all our subjects, which indicates an involvement of right-hemispheric regions as well. In various language studies with complementary methods this bi-hemispherical involvement with a preponderance of the left side could be demonstrated (Roland and Friberg, 1985; Demeurisse et al., 1991; Frith et al., 1991; Thomas et al., 1995).

4.2. Lack of frontal lateralization in patients with acute aphasia

The most interesting finding in our group of aphasics in

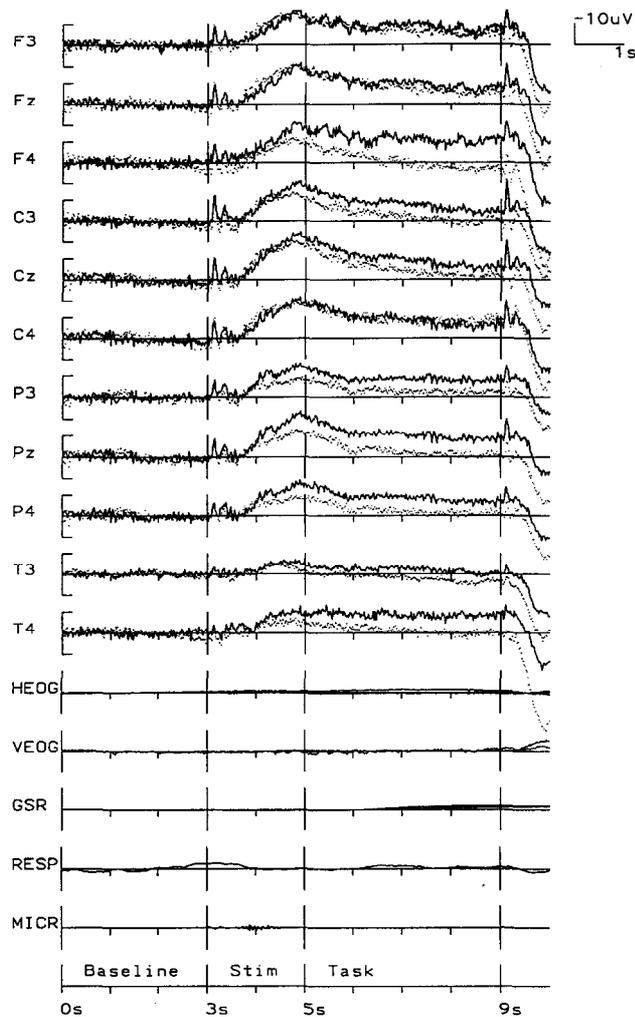


Fig. 6. Averages of a patient (L.S.) with Broca's aphasia. Solid lines represent the first measurement, the dotted line depicts the second trial.

the acute phase is the frequent occurrence of an increased right-hemispheric coactivation and even right-hemispheric preponderance which was found to be most pronounced in the right fronto-central region. Consistent with our results, a more bilateral increase was reported in rCBF during a language task (Gur et al., 1987) and in glucose metabolism during speech production (Heiss et al., 1993). This could reflect an activation or disinhibition of a homologous frontal area on the right. Homotopic regions have been shown to be linked in such a way that e.g. a receptive field expansion is immediately mirrored to the contralateral hemisphere (Calford and Tweedale, 1990) and inhibitory transcallosal pathways change their excitability during voluntary muscle action to ensure strictly unilateral movements in normal volunteers (Ferber et al., 1992). Thus, the interhemispheric inhibition of the corresponding area may be one of the mechanisms of hemispheric specialization resulting in less activation over right frontal areas in our normal subjects.

Several mechanisms are discussed for recovery in stroke. PET-data at rest demonstrating hypometabolism in various areas remote from the lesion site support the diaschisis theory by Monakow (Feeney and Baron, 1986; Karbe et al., 1989; Cappa et al., 1993), while activation studies reveal a different view. In motor recovery a bilateral activation of motor pathways and the recruitment of additional sensorimotor areas is described which is attributed to a functional disinhibition of the contralateral premotor cortex (Weiller et al., 1992). Therefore, the unmasking of the right frontal area could be due to the disinhibition by change of excitability or by destruction of transcallosal fibers connecting homologous frontal speech-related areas. Under activation conditions no diminution of amplitude sizes could be noted in our aphasic patients compared to control subjects, neither in the acute phase nor after clinical recovery. Thus, no support for the diaschisis theory can be found in our data. Our findings confirm the results of a recent PET study, assessing free associative speech production in mildly affected aphasics, that revealed an activation of the infarct zone as well as its contralateral mirror region (Heiss et al., 1993).

Most PET-studies in stroke patients suffering from aphasia, however, have been conducted under resting conditions and therefore are not directly comparable. The left temporoparietal cortex was found to be the most consistently affected region in all aphasic patients (Metter et al., 1990) and its metabolism correlated significantly with aphasia scores (Karbe et al., 1990). These findings suggest a predominant role of the left temporoparietal region in aphasia. However, these data are averaged over all aphasic patients and in our opinion reflect only areas that are commonly involved in all aphasics. Considering the remarkable inter-individual variation of essential language areas (Ojemann et al., 1989), especially in the frontal region, inter-individual averaging techniques might mask the contribution of Broca's area (Steinmetz and Seitz, 1991). In a much smaller sample of patients a right metabolic preponderance could be demonstrated in frontal regions (Metter et al., 1989). This again correlated to the patients' aphasia. The asymmetry was found to be largest in patients suffering from Broca's aphasia and was attributed to a severe left frontal dysfunction. The described patterns of asymmetry resemble the lateralization patterns observed in our study. In our paradigm, however, we did not find a lack in neuronal activity over the left frontal region in general, but an additional frontal activation on the right. Language-related rCBF increases in the right frontal region have been reported exclusively in mildly affected patients (Demeurisse et al., 1991). Their Xenon-CT-findings are consistent with our results. Only mildly affected patients, as indicated by their Token test scores, were able to solve the paradigm used in our study. More severely impaired aphasics could not be tested.

COURSE OF RECOVERY

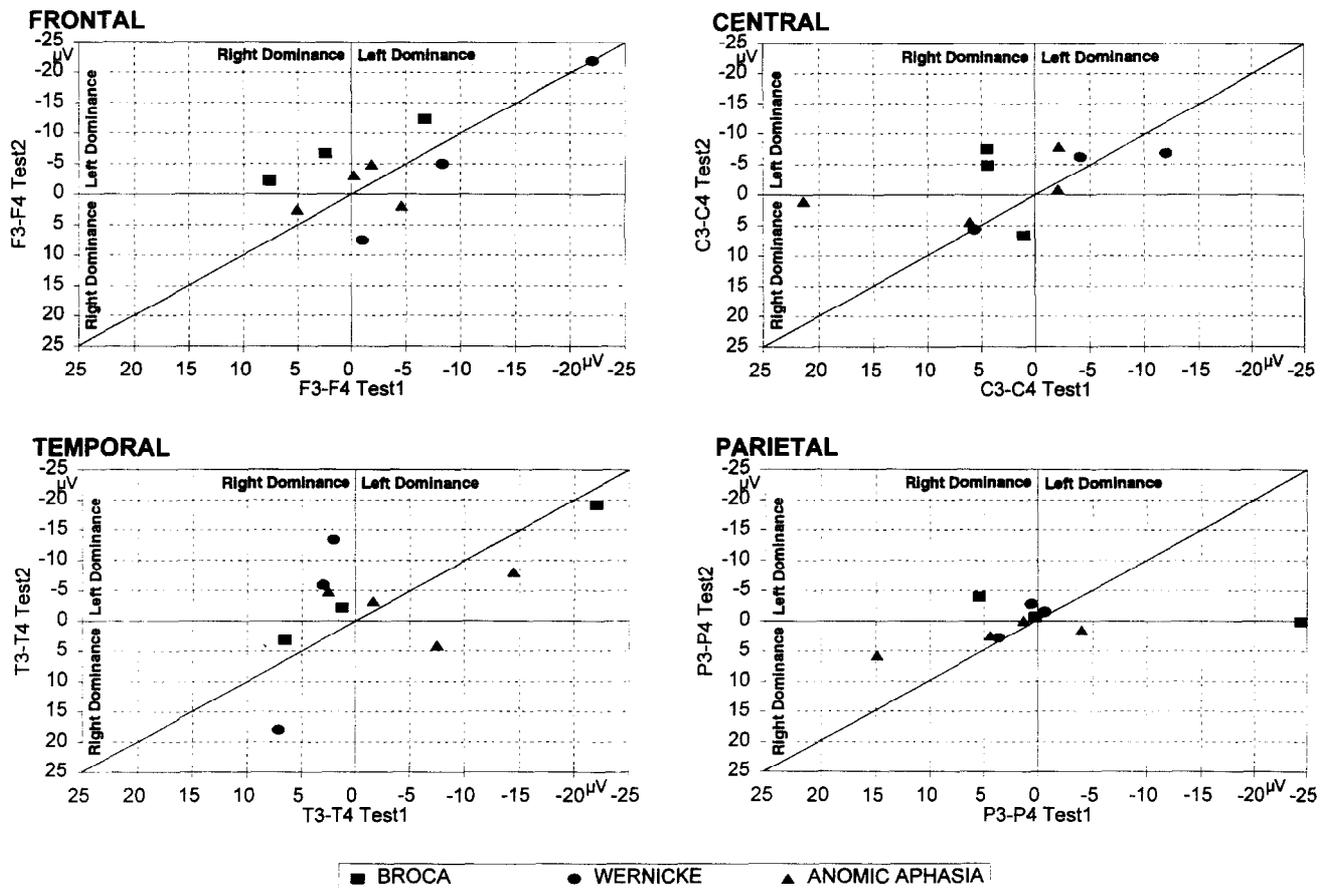


Fig. 7. Change of lateralization patterns in stroke patients during the course of recovery: Mean amplitude value differences of the first (abscissa) and second (ordinate) assessment are compared. In the frontal leads all Broca's aphasics are located above the diagonal indicating an increase in left-hemispheric predominance with two of them, as located in the left upper quadrant, even revealing a shift from initial right-hemispheric preponderance to the physiological left frontal lateralization pattern. In contrary, Wernicke's aphasics, located in the right lower quadrant, mostly reveal a shift towards the right hemisphere.

4.3. Change of lateralization patterns during recovery from aphasia

Patterns of recovery in vascular aphasia, especially in the acute phase, have rarely been evaluated (Kertesz and McCabe, 1977). Evolution of aphasia, i.e. changes in type or severity of aphasia during recovery, was thoroughly studied by Pashek and Holland (1988). These authors observed an evolutionary change in 65% of aphasics which occurred predominantly within the first month after stroke. Complete recovery occurred more often in Broca's and anomic aphasia than in Wernicke's aphasia. In our follow-up study patients were only retested if they had recovered completely. All but one of these patients changed their frontal lateralization pattern during their course of recovery. Although patient numbers are small, the differences found between the classical aphasic syn-

dromes are suggestive: Broca aphasics shift back to a lateralization towards the left hemisphere, Wernicke aphasics shift to the right. Why the right-hemispheric involvement in Broca's aphasia is transient remains to be investigated. Restoration of left-hemispheric function and thereby collateral inhibition of the right-hemispheric areas is possible.

Clinical observations on patients with Wernicke's aphasia (Cambier et al., 1983; Lee et al., 1984; Basso et al., 1989) suggest that the right-hemispheric involvement in these cases is most likely permanent. This was recently confirmed by PET-findings in patients fully recovered from Wernicke's aphasia, which showed a rCBF increase in the right superior temporal gyrus as well as the right prefrontal cortex (Weiller et al., 1995). Our results demonstrate that in sensory aphasics the right-hemispheric involvement occurs later in the course of recovery and might involve alterations in synaptic transmissions (Mendell,

1988) and the recruitment of relatively ineffective synapses (Wall, 1988). Thus, specific mechanisms of recovery could account for each of the different patterns in lateralization changes the various aphasia groups exhibit.

Cerebral glucose metabolism during a free associative speech production task has recently been postulated to be a predictor of recovery from aphasia (Heiss et al., 1993). In acute but mildly affected fluent aphasics regional metabolic rates of the infarct area, its contralateral mirror region and Broca's area were found to have the largest contribution to significant recovery as measured by a second Token test. A PET follow-up study of two cases with crossed aphasia revealed a close parallelism between cerebral glucose metabolism at rest and clinical course as well as the presence of a functional involvement of the structurally unaffected left hemisphere in the acute stage (Cappa et al., 1993).

Longitudinal rCBF-studies of right-handed aphasics have only been conducted by Knopman et al. (1984a), who also observed a transient right-hemispheric involvement along with good recovery, while patients with permanent comprehension deficits and left temporo-parietal lesions revealed a right frontal rCBF increase 6 months later in the course of their (incomplete) recovery.

Differences in recovery mechanisms according to aphasia types have also been noted by Kertesz (1988) who postulated ipsilateral, especially thalamo-frontal, structures to be important for the complete and long-term recovery of motor output, while comprehension deficits might have more contralateral or right-hemispheric compensation.

Nevertheless, it has to be emphasized that there is a high degree of inter-individual variability already in physiological language conditions that might be even more important during recovery. The individual course of recovery reflected by the high variety of evolutionary changes in aphasia (Pashek and Holland, 1988) as well as individual differences in recovery of special linguistic functions, i.e. naming (Knopman et al., 1984b), underlines the importance of individual factors in recovery from aphasia. The assessment of DC-potential shifts during single word processing represents an especially reliable method for the investigation of language recovery, as due to its non-invasiveness and intraindividual averaging procedures, exactly those individual influences on language lateralization patterns and recovery from aphasia can be taken into account.

Although these results have to be regarded as preliminary, as there are only small subgroups, the classical aphasic syndromes revealed specific differences during their course of recovery. These most interesting findings with respect to the general interpretation of mechanisms of recovery from brain lesions are supported by the results of other methodological approaches for the assessment of higher brain functions.

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