

Brain State-dependent Functional Hemispheric Specialization in Men but not in Women

Christine Mohr^{1,2}, Christoph M. Michel¹, Goran Lantz¹, Stephanie Ortigue¹, Isabelle Viaud-Delmon³ and Theodor Landis¹

¹The Functional Brain Mapping Laboratory of the Neurology Clinic, University Hospital Geneva, Geneva, Switzerland, ²Rehabilitation Clinic, University Hospital Geneva, Geneva, Switzerland and ³CNRS UMR 7593, Hopital de la Salpêtrière, Paris, France

Hemispheric specialization is reliably demonstrated in patients with unilateral lesions or disconnected hemispheres, but is inconsistent in healthy populations. The reason for this paradox is unclear. We propose that functional hemispheric specialization in healthy participants depends upon functional brain states at stimulus arrival (FBS). Brain activity was recorded from 123 surface electrodes while 22 participants (11 women) performed lateralized lexical decisions (left hemisphere processing) on neutral and emotional (right hemisphere processing) words. We determined two classes of stable FBS, one with right anterior-left posterior orientations (RA-LP maps) and one with left anterior-right posterior orientations (LA-RP maps). Results show that functional hemispheric specialization is dependent upon the class of FBS and gender. Of those with LA-RP maps, only men showed a strong emotional word advantage (EWA) after left visual field (right hemisphere) presentation, but no EWA after right visual field (left hemisphere) presentation. Subsequent to all other brain states, there was an almost equal EWA after presentation to either visual field. Only about half of the FBS in men led to the pattern of functional hemispheric specialization. We suggest that 'split-brain' research may be marginally describable by a model, but only in exceptional situations, while in connected brains this functional hemispheric specialization is only one of many dynamic states.

Keywords: EEG, emotion, gender differences, lateralization, lexical decision

Introduction

The concept of hemispheric specialization or 'cerebral dominance' derives from clinical observations on patients with unilateral cerebral lesions. As early as in the mid-1800s, the left hemisphere (LH) was found to be 'dominant' for language (Broca, 1865; Wernicke, 1874). 'Dominance' of the right hemisphere (RH) was later postulated for functions such as face-identification (Hoff and Pötzl, 1937; Hécaen and Angelergues, 1962), affective, prosodic and intonational aspects of spoken language (Hughling Jackson, 1876; Ross, 1981), emotional word processing (Goodglass *et al.*, 1980), space perception and exploration (Poppelreuter, 1917; Kleist, 1923), and topographic orientation (Hughling Jackson, 1876; Pommé and Janny, 1954). Additionally, during the nineteenth century, concepts about hemispheric interactions, such as inhibition (Wigan, 1844; Hughlin Jackson, 1874) and functional disconnection (Wernicke, 1874; Dejerine, 1892; Liepmann, 1900), were introduced. However, only with the 're-discovery' of the classical disconnection syndromes in patients (Geschwind, 1965a,b) and experimental discoveries on hemispheric specialization obtained from split-brain patients (Sperry *et al.*, 1969) did the disconnection approach become the cornerstone of current ideas about hemispheric functional

specialization. This left brain/right brain dichotomy has consequently entered common knowledge well beyond the scientific community (Springer and Deutsch, 1981).

Various kinds of functional hemispheric dominance are typically found when testing split-brain patients or those with unilateral cortical lesions, but not when testing healthy populations (e.g. Blumstein *et al.*, 1975; Satz, 1977; Teng, 1981; Bryden, 1982; Corballis, 1983; Hiscock *et al.*, 2000). The behavioral results from this laterality research in healthy populations using many different experimental paradigms and a wide variety of stimuli showed an unexpected variability, if not unreliability, of results. No single lateralized experimental procedure has been established that is able to predict with certainty the most prevalent form of hemispheric dominance, i.e. left hemispheric language dominance, in a single healthy individual. Moreover, group studies have shown functional hemispheric specialization to a much lesser degree than expected from patient studies, and different lateralized measures obtained from the same population correlate only weakly with each other (e.g. Teng, 1981; Graves, 1983; Boles, 2002). For language tasks, right visual field (RVF) or right ear advantages are unstable within one individual at two time points of experimentation (Blumstein *et al.*, 1975; Teng, 1981). Non-verbal material has been shown to shift from a left-to-right hemisphere advantage over time, as if a 'mental set' gets established (Turkewitz and Ross, 1983; Kinsbourne and Bruce, 1987; Hiscock *et al.*, 1996). This variability and inconsistency of laterality results in healthy subjects remain unexplained (e.g. Hiscock *et al.*, 2000; Hugdahl, 2000; Josse and Tzourio-Mazoyer, 2004) and many researchers have left the field (Efron, 1990).

One major difference between healthy subjects and patients is that in the former the corpus callosum is intact, allowing for cross talk between the hemispheres. In split-brain patients, the cross talk is abolished, and in patients with unilateral cortical lesions, transcallosal fibers are damaged and as a consequence interhemispheric cross talk is impaired, at least for anatomically homotopic areas. Thus, in clinical populations with interrupted interhemispheric information transfer, it is likely that the two hemispheres process incoming information according to their specialization, uninfluenced by the contralateral processing (for an overview, see Gazzaniga, 2000). In contrast, in healthy populations with interactive hemispheres, hemispheric dominance patterns can vary according to situational/attentional factors (e.g. Spellacy and Blumstein, 1970; Hiscock and Kinsbourne, 1977; Hugdahl, 2000) or individual electrophysiological asymmetries (Davidson and Hugdahl, 1996). Thus, both hemispheres can process incoming information, but which hemisphere will be dominant for this processing might depend on the individual's processing style favored at the moment of stimulus arrival. What

we suggest by this proposition is that the momentary 'brain state' at stimulus arrival might be a crucial determinant of the fate of subsequent information processing (Koukkou and Lehmann, 1987), and might thus determine whether the current sensory information is preferentially transferred to and/or processed by one or the other hemisphere. In order to test this hypothesis, one has to find means of (i) measuring brain states at the time of stimulus arrival and (ii) defining behaviorally what one would assume to be a 'favored' hemispheric processing style, i.e. a relative left or right hemisphere strategy of stimulus processing.

With respect to the first requirement, functional brain states at stimulus arrival (FBS) can be defined electrically by means of the momentary configuration of the global scalp electric potential, reflecting the momentary neuronal cerebral activity. Topographic differences in such global scalp electric potentials at stimulus arrival directly indicate that different neuronal populations are active. It is reasonable to assume that different distributions of active neuronal populations serve different functions, and thus represent different momentary functional states of the brain (Koukkou and Lehmann, 1987). These momentary states, when defined as periods of topographic stability of the electric potentials, last for ~80–150 ms and presumably correspond to spontaneous coherent functional microstates of the brain (Lehmann, 1987; Wackermann *et al.*, 1993; Koenig *et al.*, 2002). In previous work, Lehmann and collaborators (Lehmann *et al.*, 1994; Kondákor *et al.*, 1995, 1997) have classified these functional microstates just prior to stimulus presentation and calculated separate evoked-potentials for each class. The authors showed that stimulus-evoked potentials drastically varied as a function of such different classes of functional microstates at stimulus arrival, independent of task complexity. Similarly, evoked magnetic field differences have been described in dependence of the complexity of the magnetic field before stimulus onset (Braeutigam and Swithenby, 2003). These findings are closely related to electrophysiological studies that showed correlations of neuronal activity patterns before the appearance of a stimulus with subsequent perceptual decisions or behavioral events. These pre-stimulus activity patterns are expressed either as the amount of discharges of primary sensory neurons (Super *et al.*, 2003) or as synchrony of local field potentials between different sites in the brain (Engel *et al.*, 2001; Gonzalez-Andino *et al.*, 2004). In summary, these studies indicate that subtle variations of the FBS influence subsequent event-related information processing following common rules across subjects. Based on these findings, we hypothesize that functional hemispheric specialization within a given healthy population may depend on such classes of FBS.

With respect to the second requirement, hemispheric differences in information processing can be measured in terms of right (RVF) or left visual field (LVF) advantages in tachistoscopic paradigms. Based on previous findings (Graves *et al.*, 1981), we decided to use a lexical decision task on neutral and emotional words in a simultaneous bilateral visual field presentation paradigm. Graves *et al.* (1981) observed an overall RVF advantage for lexical decisions and an overall advantage for emotional over neutral words (see also Ortigue *et al.*, 2004). More importantly for the present study, this emotional word advantage (EWA) was significantly stronger after LVF than RVF presentation due to an above-chance performance for emotional words and an at-chance performance for neutral words (Graves *et al.*, 1981). However, this visual-field difference turned out to be specific for men but not for women. These results support a specific role of

the right hemisphere for emotion perception in general (e.g. Borod *et al.*, 2001; Adolphs, 2002) and emotional word processing in particular (Graves *et al.*, 1981; Windmann *et al.*, 2002; Taylor and Regard, 2003), at least in male populations. We will refer to the EWA of the LVF as a 'right hemispheric strategy' and to the strength of RVF performance (no advantage for emotional over neutral words) as a 'left hemispheric strategy'. The co-existence of both strategies will be considered as 'functional hemispheric specialization', since each strategy favors the dominance of a specific hemisphere for a given function.

The aim of the present study was to evaluate whether the selection for one or the other strategy depends on FBS. Moreover, since a 'right hemispheric' versus 'left hemispheric' strategy appears to be more pronounced in men than women, we tested an equal number of female and male participants. Therefore, if our hypothesis holds, the state-dependent information processing effect should be more pronounced in men than women.

Materials and Methods

Twenty-two paid healthy participants (11 women), aged 18–36 years [women: 24.6 ± 3.4 years, men: 27.3 ± 5.2 years; unpaired *t*-test: $t(10) = 1.40$, $P = 0.18$], provided written informed consent to participate in the experiment, which was approved by the Medical ethics committee at the University Hospital of Geneva. All were right-handed (Edinburgh Inventory; Oldfield 1971), native French speakers with normal or corrected-to-normal vision and no neurological or psychiatric illnesses.

Experimental Procedure

The 112 letter-string stimuli (four to seven characters in length) included eight French emotional abstract nouns [e.g. *colère* (anger), *espoir* (hope)], eight French neutral abstract nouns [e.g. *chose* (thing), *ligne* (line)] and 96 pronounceable nonwords (for details on word selection, see Ortigue *et al.*, 2004). Letter-strings were presented in pairs — one on either side of central fixation (spanning ~2–5° eccentricity) in the LVF and RVF, respectively, in a go/no-go paradigm. Words, when present, were always paired with nonwords and could appear randomly on either side of fixation, but with equal overall likelihood across the experiment. Each word appeared three times in each visual field per block of trials. The order of experimental trials was pseudorandom and implicated the constraint that no more than three consecutive trials with the same word type appeared in the same visual field. Stimuli appeared white on black for 13 ms (as confirmed by photocell measurement) on a computer monitor (E-prime Psychology Software Tools Inc.) located 140 cm from the subject, whose head was held in a chin rest. Without being aware of the emotional content of the words, subjects were instructed to decide whether one of the two letter strings was a word or not. They had to centrally fixate and judge whether or not a word was present and, if so, on which side it appeared. That is, if they believed a word was presented, they pressed a button as quickly as possible with their index finger of the hand on the same side of the fixation cross as the word (go-trials). No-go trials involved presentation of two nonwords and required no button-press. The inter-stimulus interval varied randomly between 1500–2000 ms. Subjects completed five blocks, each containing 120 trials. Each block consisted of 24 nonword/nonword pairs, 48 word/nonword pairs and 48 nonword/word pairs. Prior to inclusion in this study, potential subjects completed a training session comprised of a shortened version of the five blocks of stimuli described above, but with different word and nonword stimuli. Inclusion in the experiment required a minimum of 50% accuracy on each condition.

EEG Acquisition and Analysis

Continuous EEG was acquired with a Geodesics Netamps system (Electrical Geodesics, Inc., USA) from 123 scalp electrodes (impedance <50 k Ω ; vertex reference; 500 Hz digitization; band-pass filtered 0.01–200 Hz) as subjects performed the lexical decision task in a darkened, electrically shielded booth. The EEG epochs from each subject were visually inspected to reject epochs with blinks, eye movements, or other

sources of transient noise in addition to the application of an automated artifact criterion of $\pm 100 \mu\text{V}$. For each subject, the electrodes on the lowest raw (chin and neck) were excluded and artifact channels were interpolated (spherical spline, Perrin *et al.*, 1987) using standard electrode positions. The resulting standardized 111-channel EEG was band-pass filtered (1–30 Hz) and recalculated against the average reference.

Determination of FBS at Stimulus Arrival

The spontaneous functional microstates, measured as a certain stable electric potential topography, last for ~80–150 ms (Wackermann *et al.*, 1993; Koenig *et al.*, 2002). During a period of stable electric potential topography, only the electric strength of the field varies, but not the topography. Therefore, the best representative time point (in terms of signal-to-noise ratio) for a given stable electric potential topography is at the moment of maximal field strength (Lehmann *et al.*, 1994). A one-number measure of field strength is the global field power (GFP; Lehmann and Skrandies 1980). The GFP is measured as the square root of the mean of the squared potentials recorded at each electrode (versus the average reference), i.e. as the spatial standard deviation of the scalp electric field. The time point of maximal GFP was determined in a time window from –20 to 20 ms around stimulus onset. The electric potential topography at this time point was kept for further analysis as representing the electric manifestation of a given functional microstate at stimulus onset (the FBS map).

The FBS maps of all single trials of correct responses ($n = 5102$) were then subjected to a *k*-means cluster analysis that determines the most dominant classes of electric field configurations (Pascual-Marqui *et al.*, 1995). A cross-validation criterion was applied to define the optimal number of FBS maps (Pascual-Marqui *et al.*, 1995). Using a spatial correlation analysis (e.g. Michel *et al.*, 1999), each individual sweep was then labeled as belonging to the FBS map it best correlated with. In a last step, these FBS maps were further grouped together on the basis of the position of the positive and negative extrema of the FBS map. Based on previous studies (Lehmann *et al.*, 1994; Kondákor *et al.*, 1995, 1997), two classes were defined, one class having a left anterior–right posterior location of the extrema (LA-RP map) and the other class having a right anterior–left posterior position of the extrema (RA-LP map).

Data Analysis

Across the five blocks, artifact-free epochs for correct lexical decisions are shown in Table 1. The number of trials varied between participants and word types; thus, we calculated individuals' percent correct responses for each experimental task condition. First, we summed for each individual all artifact-free and correct trials for each FBS map class separately. This sum score was used for each FBS class as individuals' reference to calculate percent correct responses for each word type in the LVF and RVF. Consequently, a value of 25% indicates that within a given FBS class, an equal proportion of emotional and neutral words in the LVF and RVF, respectively, were correctly recognized. Relative strength of one word type over the other can be expressed by conventional index scores. We therefore calculated an index reflecting an emotional (*E*) over neutral (*N*) word advantage for each visual field separately [EWA index = $(E - N)/(E + N) \times 100$; Marshall, 1975]. Positive values indicate an EWA and negative values a neutral word advantage.

Table 1

Mean \pm SD number of functional microstate frequencies in the two FBS classes

	Total	Men		Women	
		LA-RP maps	RA-LP maps	LA-RP maps	RA-LP maps
ELVF	66.0 \pm 15.9	37.7 \pm 15.4	29.4 \pm 10.4	26.7 \pm 7.0	38.2 \pm 12.8
NLVF	40.1 \pm 13.9	23.0 \pm 17.2	18.3 \pm 5.3	17.4 \pm 6.4	21.6 \pm 6.1
ERVf	87.8 \pm 18.6	42.2 \pm 18.0	42.7 \pm 11.9	38.1 \pm 8.2	52.5 \pm 14.4
NRVf	67.5 \pm 17.8	40.5 \pm 18.9	29.8 \pm 11.0	26.0 \pm 8.0	38.6 \pm 11.4
Total	261.4 \pm 54.6	143.5 \pm 65.2	120.2 \pm 31.2	108.2 \pm 21.6	151.0 \pm 41.0

Values are presented for emotional (E) and neutral (N) words in the left-visual field (LVF) and right-visual field (RVF) for women and men separately as well as across all 22 participants.

Furthermore, to specify whether lexical decision performance is dependent on the two classes of FBS topographies, we determined EWA index scores for the LA-RP maps and RA-LP maps separately. These EWA index scores were subjected to a three-way analysis of variance (ANOVA) with gender as between-subject measure and class of FBS topography (LA-RP maps versus RA-LP maps) and visual field (RVF, LVF) as repeated measures. All post-hoc comparisons, if not otherwise stated, were performed with Scheffé tests. The *P*-values are two-tailed and the alpha-level was set at 0.05.

Results

A two-way ANOVA with word type (emotional, neutral) and visual field (LVF, RVF) as repeated measures on percent correct lexical decisions replicated previous findings (Graves *et al.*, 1981; Ortigue *et al.*, 2004; Strauss, 1983) of an overall advantage for emotional (29.5 ± 2.2) over neutral (20.5 ± 2.2) words [$F(1,21) = 92.76$, $P < 0.0001$] and for the RVF (29.8 ± 2.5) over the LVF (20.2 ± 2.5) [$F(1,21) = 77.31$, $P < 0.0001$].

Determination of the Two Classes of FBS Maps

The cross-validation criteria revealed that 12 different FBS maps best explain all the different FBS. These 12 FBS maps are shown in Figure 1. As can be seen, half of the FBS maps are characterized by LA-RP orientations of the extrema while the other half show RA-LP orientations. Visual inspection of the FBS maps indicates that the spatial topography of the FBS not only varies between FBS classes, but also within the FBS maps of a given FBS class (Fig. 1). Nevertheless, the median spatial correlation when comparing the six LA-RP maps with each other (median $r = 0.63$) or the six RA-LP maps (median $r = 0.66$) was higher than the mean correlation when comparing FBS maps belonging to the two different FBS classes (median $r = 0.36$). An ANOVA with gender as between-subject measure and number of maps (LA-RP, RA-LP) as repeated measures showed (i) that FBS maps were equally frequent in women and men [$F(1,20) = 0.03$, $P = 0.85$]; (ii) that LA-RP maps (125.82 ± 50.69) were as frequent as RA-LP maps (135.59 ± 38.88) [$F(1,20) = 0.50$, $P = 0.49$]; and (iii) there was a significant interaction between gender and number of maps [$F(1,20) = 5.67$, $P = 0.03$]. Although all the Scheffé comparisons were non-significant (all *P*-values > 0.20), Table 1 shows that men had more LA-RP maps and women had more RA-LP maps. In Table 1, we also present the absolute numbers in men and women of artifact-free EEG epochs of correct lexical decisions for emotional and neutral words presented to the LVF and RVF as a function of the class of FBS maps.

Percent correct trials and EWA index scores for each task condition are presented in Table 2. The planned ANOVA on the EWA index score indicated a significant main effect for visual fields [$F(1,20) = 24.76$, $P < 0.0001$]; the emotional word advantage was higher after LVF (25.1 ± 13.4) than after RVF (9.8 ± 9.8) presentation. The interaction between visual field and gender just failed to reach the conventional significance level [$F(1,20) = 3.50$, $P = 0.08$]. The present study deals with inconsistencies within and between studies when testing hemispheric specialization in healthy populations. Thus, we feel that it is legitimate to break down the interaction presenting post-hoc analysis, in particular since this type of significant interaction was found on one previous occasion (Graves *et al.*, 1981) and once as a statistical trend (Strauss, 1983). In line with these previous two studies, men showed a stronger EWA after LVF (25.4 ± 12.7) than RVF (9.8 ± 9.5) presentation ($P = 0.001$),

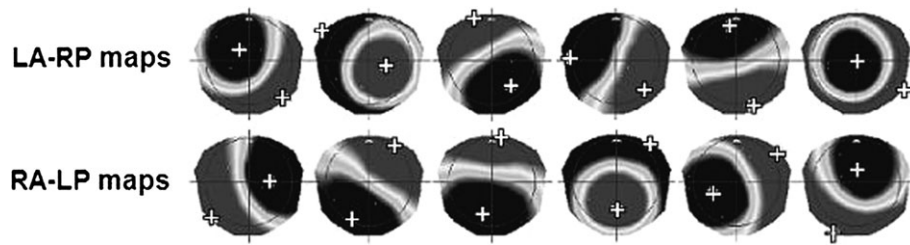


Figure 1. The 12 FBS maps determined from the spatial cluster analysis. Shown in the upper row are the six FBS maps with a left anterior–right posterior orientation of the extrema (LA-RP maps) and in the lower row those with a right anterior–left posterior orientation (RA-LP maps).

Table 2

Mean \pm SD percent correct trials and EWA index scores are shown for LA-RP maps and RA-LP maps as a function of word type after left-visual field (LVF) and right-visual field (RVF) presentation for the gender groups, separately

	FBS class	Females		Males	
		LVF	RVF	LVF	RVF
Emotional words	LA-RP maps	24.9 \pm 4.4	35.6 \pm 5.7	26.9 \pm 5.5	29.8 \pm 4.8
Neutral words		15.9 \pm 4.0	23.7 \pm 4.2	14.9 \pm 5.7	28.4 \pm 4.8
EWA index		22.6 \pm 12.7	20.0 \pm 12.7	29.7 \pm 19.9	2.3 \pm 9.7
Emotional words	RA-LP maps	25.0 \pm 3.1	34.9 \pm 3.6	24.1 \pm 4.8	35.6 \pm 4.4
Neutral words		14.4 \pm 2.4	25.6 \pm 3.4	15.6 \pm 4.4	24.7 \pm 4.9
EWA index		26.7 \pm 11.1	15.4 \pm 10.2	21.5 \pm 18.5	18.4 \pm 13.1

while women did not differ between visual fields (RVF: 17.0 \pm 9.0; LVF: 24.0 \pm 6.2; $P = 0.22$; see Fig. 2).

The three-way interaction between gender, class of FBS topography and visual field was also significant [$F(1,20) = 9.38$, $P = 0.006$]. We calculated the same ANOVAs as before, but for the two classes of FBS topographies separately. The ANOVA for RA-LP maps showed a statistical trend for visual fields [$F(1,20) = 3.88$; $P = 0.06$; LVF > RVF: 24.1 \pm 15.11 > 16.9 \pm 11.5]. The main effect for gender [$F(1,20) = 0.06$, $P = 0.81$] and the interaction between gender and visual fields [$F(1,20) = 1.23$, $P = 0.28$] were both not significant. The ANOVA for LA-RP maps showed a significant main effect for visual field [$F(1,20) = 20.35$, $P = 0.0002$] and a significant interaction between gender and visual field [$F(1,20) = 13.96$, $P = 0.001$]. The visual field difference resulted from a significantly stronger EWA after LVF (26.1 \pm 16.7) than RVF (11.1 \pm 14.3) presentation. The significant interaction between gender and visual field indicated that this visual field difference was due to the male but not female participants. While women did not differ in their EWA after LVF or RVF presentation ($P = 0.96$), men showed a strongest EWA after LVF and no EWA after RVF presentation ($P = 0.0001$; see Fig. 3). The main effect for gender was not significant [$F(1,20) = 1.08$, $P = 0.31$].

Discussion

There is a distinction between ‘clear cut’ signs of cerebral dominance in ‘split-brain’ patients or patients with unilateral cerebral lesions and the relative unreliability of these ‘dominance’ measures in healthy subjects. In contrast to the clinical populations, healthy participants do not suffer from direct or indirect damage to the major interhemispheric fiber tract, the corpus callosum. An intact corpus callosum allows interhemispheric information transfer in the millisecond range (Poffenberger, 1912; Aboitiz *et al.*, 2003). Thus, even minor events such as random changes in the FBS might influence

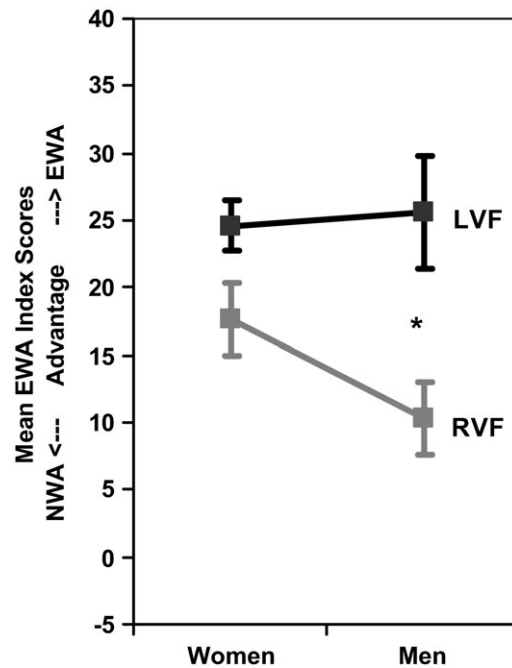


Figure 2. Mean EWA index scores for correct lexical decisions after word presentation to the RVF and LVF. Positive values indicate an emotional word advantage (EWA) and negative values a neutral word advantage (NWA). Index scores are displayed for the two gender groups separately. A star indicates significant differences and vertical bars indicate standard errors.

subsequent information processing (Koukkou and Lehmann, 1987; Braeutigam and Swithenby, 2003). To test the idea that FBS determine subsequent hemispheric specialization, healthy participants performed a lateralized lexical decision task on emotional and neutral words while their brain activity was continuously recorded from 123 surface electrodes.

The main results of the present study are that (i) FBS influenced subsequent hemispheric specialization, but only in men and not in women; and (ii) in men, only the LA-RP maps appeared to induce a ‘functional hemispheric specialization’, while RA-LP maps resulted in an EWA advantage for both visual fields alike, identical to that of women found across FBS.

In earlier studies, it has been shown that FBS influence subsequent information processing as evidenced by differences in visual (Kondákor *et al.*, 1995, 1997) and auditory (Lehmann *et al.*, 1994) event-related potentials. In these studies, FBS were defined electrically in terms of systematic topographic differences in global scalp electric potentials. The topographies of these potentials were observed to have most frequently diagonal orientations with either a left anterior–right posterior

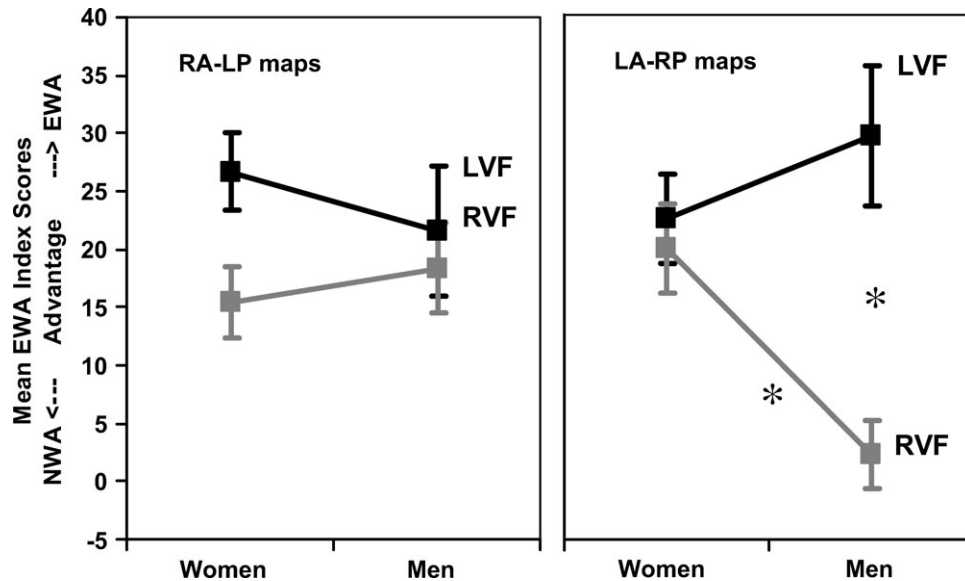


Figure 3. Mean EWA index scores for correct lexical decisions after word presentation to the right visual field (RVF) and left visual field (LVF). Positive values indicate an emotional word (EWA) advantage and negative values a neutral word (NWA) advantage. Index scores are displayed for the two gender groups and classes of FBS maps separately. A star indicates significant group differences and vertical bars indicate standard errors.

orientation (LA-RP maps) or a right anterior-left posterior orientation (RA-LP maps). In the present study, we likewise determined these two classes of FBS maps and found that behavioral hemispheric specialization differed subsequent to these two classes of FBS maps. In men only, behavior after LA-RP maps showed a strong EWA after LVF stimulus presentation and no difference between emotional and neutral words after RVF stimulus presentation. The striking EWA after LVF presentation resulted from an excellent emotional word recognition (in the range of RVF-LH lexical decision), but even more so from the lowest recognition of neutral words (see Table 2). In all other conditions, i.e. men subsequent to RA-LP maps as well as women after LA-RP maps and RA-LP maps, behavior was similar showing a slight EWA for LVF over RVF presentation (see Fig. 3).

Thus only men after LA-RP maps showed hemispheric asymmetry, as expected from the literature on the divided brain. In fact, the literature on 'split-brain' and unilaterally lesioned patients shows dominance for language in the left hemisphere (for an overview, see Gazzaniga, 2000) and a specific role of the right hemisphere for emotion perception in general (e.g. Borod *et al.*, 2001; Adolphs, 2002) and emotional word processing in particular (Graves *et al.*, 1981; Windmann *et al.*, 2002; Taylor and Regard, 2003). In earlier studies, in which the same experimental paradigm as in the present study was used (though in English), a strong EWA for words presented to the LVF was observed in men but not in women (Graves *et al.*, 1981). In parallel, male aphasic patients with damaged left but intact right hemispheres, tested with the same emotional and neutral words, showed a strong EWA in reading and writing (Landis *et al.*, 1982). An item comparison of these two experiments showed no correlation for the RVF performance between healthy men and aphasic patients. However, a strong correlation was observed for the LVF performance between these two populations (Goodglass *et al.*, 1980). These findings show two distinct reading strategies, one dependent whether the stimuli were words in general (left hemispheric reading strategy) and

one dependent on their emotional content (right-hemispheric reading strategy). Moreover, they demonstrate a functional hemispheric specialization phenomenon in healthy men, since two distinctly different reading processes take place in parallel. The present experiment shows this dissociation to a much stronger degree than observed from the previous studies in healthy men (Graves *et al.*, 1981; Ortigue *et al.*, 2004; Strauss, 1983), but only in about half of the instances of stimulus presentation, i.e. when they performed lexical decisions after LA-RP maps. It thus appears that in healthy men some early momentary electric brain states will induce functional hemispheric specialization while others allow an EWA in general. This phenomenon is dynamic in the sub-second range and ongoing over time.

Our observation of 'functional hemispheric specialization' in men but not women may help clarify issues concerning gender differences in cerebral hemispheric specialization. Compared with men, women yielded fewer if any lateral asymmetries in behavioral (McGlone, 1980; Halpern, 1986; Hough *et al.*, 1994; Meinschaefer *et al.*, 1999), neuroimaging (Shaywitz *et al.*, 1995; Rossell *et al.*, 2002) and anatomical (Wada *et al.*, 1975; Kulynych *et al.*, 1994; Shapleske *et al.*, 1999; Amunts *et al.*, 2000) studies. Such gender differences are supported by results obtained from patients with unilateral cerebral lesions (McGlone, 1977; Inglis and Lawson, 1981; Grabowska *et al.*, 2001). Recovery from aphasia is better in women than in men, presumably due to a more bihemispheric representation of language functions (Pizzamiglio *et al.*, 1985; Frith and Vargha-Khadem, 2001). However, several studies have questioned the stability of a more symmetrically organized brain in women. They rather propose hemispheric specialization to depend on hormonal variations during the menstrual cycle. In fact, cognitive skills vary during the menstrual cycle of normal healthy women (Hampson and Kimura, 1988; McCormick and Teillon, 2001), indicating left hemisphere advantages when estradiol and/or progesterone levels are high (midluteal, ovulatory phase) and right hemisphere

advantages when estradiol and progesterone levels are low (menstrual phase). Independent studies using lateralized stimulus presentation tasks confirm such fluctuating hemispheric dominance patterns during the menstrual cycle (Heister *et al.*, 1989; Hausmann and Güntürkün, 2000; Purdon *et al.*, 2001). Unfortunately, we did not control for hormonal levels or time of menstrual cycle in our present study. Nevertheless, we would predict that women's performance would become similar to that of men when the time of testing is controlled for menstrual cycle. In particular, during the menstrual phase, when estradiol and progesterone levels are low, functional hemispheric specialization subsequent to LA-RP maps in women might be similar to that seen in men.

Our experiment was based on the hypothesis that early electric brain states (FBS) might explain inconsistent results of research on hemispheric specialization in healthy subjects. Theory-based models to account for our results would be premature and highly conjectural. We could show that FBS influence later stimulus processing, but a basic question to test is whether FBS relate systematically to experimental and person variables or whether they are of random occurrence. Both situations, however different, have testable implications for models such as that of different 'mental sets' (Kinsbourne and Bruce, 1987) or 'general processing strategies' (Turkewitz and Ross, 1983). Selective attention to certain stimulus features (emotional and neutral word recognition in one or the other hemifield in the present case) might modulate cerebral baseline activity in task-sensitive areas (Chawla *et al.*, 1999) as a function of the spatial attention allocation to either one hemifield (Müller *et al.*, 2003; Giabbiconi *et al.*, 2004) or when divided between different spatial locations (Awh and Pashler, 2000; Müller *et al.*, 2003). FBS might also relate to different 'motivational/emotional' states over time (Harmon-Jones and Allen, 1997; Davidson, 2004). Moreover, FBS might play a role in models on hemispheric specialization, such as that of 'interhemispheric inhibition' (Wigan, 1844; Cook, 1986; Regard *et al.*, 1994; Hilgetag *et al.*, 2001) or that of 'direct access versus callosal relay' (Zaidel, 1983). This latter model is of particular interest with regard to our findings, especially in men. In the 'direct access' condition, the two hemispheres treat the information in their own processing style. In the 'callosal relay' condition, the 'dominant' hemisphere deals with the information, irrespective of the visual field of presentation. This appears exactly what the two classes of FBS induced. Finally, it has to be questioned what the biological advantage of such a mechanism might be. If hemispheric specialization is entirely stimulus driven, the two hemispheres would become so highly specialized that they would lose omnipotentiality, i.e. the potential to treat any kind of information, even that for which they are not specialized (Sperry *et al.*, 1969). FBS could be a mechanism which, possibly by modulating inhibitory or excitatory connectivity of the corpus callosum, could prevent the loss of this potential.

Notes

We thank Denis Brunet for expertise in designing and programming CarTool software, and Norman D. Cook and Roger E. Graves for their helpful comments on an earlier version of this manuscript. Additionally, we much appreciate Tom Troscianco's editorial advice. This work was supported by a grant from the Swiss National Research Foundation (#31-65096.01).

Address correspondence to Christine Mohr, Ph.D., Department of Experimental Psychology, University of Bristol, 8 Woodland Road, Bristol BS8 1TN, UK. Email: Christine.Mohr@bristol.ac.uk.

References

- Aboitiz F, Lopez J, Montiel J (2003) Long distance communication in the human brain: timing constraints for inter-hemispheric synchrony and the origin of brain lateralization. *Biol Res* 36:89-99.
- Adolphs R (2002) Recognizing emotion from facial expressions: psychological and neurological mechanisms. *Behav Cogn Neurosci Rev* 1:21-62.
- Amunts K, Jancke L, Mohlberg H, Steinmetz H, Zilles K (2000) Interhemispheric asymmetry of the human motor cortex related to handedness and gender. *Neuropsychologia* 38:304-312.
- Awh E, Pashler H (2000) Evidence for split attentional foci. *J Exp Psychol Hum Percept Perform* 26:834-846.
- Blumstein S, Goodglass H, Tartter V (1975) The reliability of ear advantage in dichotic listening. *Brain Lang* 2:226-236.
- Boles DB (2002) Lateralized spatial processes and their lexical implications. *Neuropsychologia* 40:2125-2135.
- Borod JC, Zgaljardic D, Tabert MH, Koff E (2001) Asymmetries of emotional perception and expression in normal adults. In: *Emotional behavior and its disorders*, pp. 181-205. (Gainotti G, ed.). Oxford, UK: Elsevier Science.
- Braeutigam S, Swithenby SJ (2003) Endogenous context for visual processing of human faces and other objects. *Neuroreport* 14:1385-1389.
- Broca P (1865) Sur le siège de la faculté du langage articulé. *Bull Soc Anthropol* 6:377-393.
- Bryden MP (1982) *Lateralality: functional asymmetry in the intact brain*. New York: Academic Press.
- Chawla D, Rees G, Friston KJ (1999) The physiological basis of attentional modulation in extrastriate visual areas. *Nat Neurosci* 2:671-676.
- Cook ND (1986) *The brain code: mechanisms of information transfer and the role of the corpus callosum*. London: Methuen.
- Corballis MC (1983) *Human laterality*. New York: Academic Press.
- Davidson RJ (2004) What does the prefrontal cortex 'do' in affect: perspectives on frontal EEG asymmetry research. *Biol Psychol* 67:219-233.
- Davidson RJ, Hugdahl K (1996) Baseline asymmetries in brain electrical activity predict dichotic listening performance. *Neuropsychology* 10:241-246.
- Dejerine J (1892) Contribution à l'étude anatomo-pathologique et clinique des différentes variétés de cécité verbale. *CR Séances Mém Soc Biol* 44:61-90.
- Efron R (1990) *The decline and fall of hemispheric specialization*. Hillsdale, NJ: Lawrence Erlbaum Associates.
- Engel AK, Fries P, Singer W (2001) Dynamic predictions: oscillations and synchrony in top-down processing. *Nat Rev Neurosci* 2:704-716.
- Frith U, Vargha-Khadem F (2001) Are there sex differences in the brain basis of literacy related skills? Evidence from reading and spelling impairments after early unilateral brain damage. *Neuropsychologia* 39:1485-1488.
- Gazzaniga MS (2000) Cerebral specialization and interhemispheric communication: does the corpus callosum enable the human condition? *Brain* 123:1293-1326.
- Geschwind N (1965a) Disconnexion syndromes in animals and man. I. *Brain* 88:237-294.
- Geschwind N (1965b) Disconnexion syndromes in animals and man. II. *Brain* 88:585-644.
- Giabbiconi CM, Dancer C, Zopf R, Gruber T, Müller MM (2004) Selective spatial attention to left or right hand flutter sensation modulates the steady-state somatosensory evoked potential. *Brain Res Cogn Brain Res* 20:58-66.
- Gonzalez-Andino SL, Michel CM, Thut G, Landis T, Grave de Peralta R (2004) Prediction of response speed by anticipatory high frequency (gamma band) oscillations in the human brain. *Hum Brain Mapp* 24:50-58.
- Goodglass H, Graves R, Landis T (1980) Le rôle de l'hémisphère droit dans la lecture. *Rev Neurol* 136:669-673.
- Grabowska A, Nowicka A, Szymanska O, Szatkowska I (2001) Subjective contour illusion: sex-related effect of unilateral brain damage. *Neuroreport* 12:2289-2292.

- Graves R (1983) Mouth asymmetry, dichotic ear advantage and tachistoscopic visual field advantage as measures of language lateralization. *Neuropsychologia* 21: 641-649.
- Graves R, Landis T, Goodglass H (1981) Laterality and sex differences for visual recognition of emotional and non-emotional words. *Neuropsychologia* 19:95-102.
- Halpern DF (1986) Sex differences in cognitive abilities. Hillsdale, NJ: Lawrence Erlbaum Associates.
- Hampson E, Kimura D (1988) Reciprocal effects of hormonal fluctuations on human motor and perceptual-spatial skills. *Behav Neurosci* 102:456-459.
- Harmon-Jones E, Allen JJ (1997) Behavioral activation sensitivity and resting frontal EEG asymmetry: covariation of putative indicators related to risk for mood disorders. *J Abnorm Psychol* 106: 159-163.
- Hausmann M, Güntürkün O (2000) Steroid fluctuations modify functional cerebral asymmetries: the hypothesis of progesterone-mediated interhemispheric decoupling. *Neuropsychologia* 38:1362-1374.
- Hécaen H, Angelergues R (1962) Agnosia for faces (prosopagnosia.) *Arch Neurol* 7:92-100.
- Heister G, Landis T, Regard M, Schroeder-Heister P (1989) Shift of functional cerebral asymmetry during the menstrual cycle. *Neuropsychologia* 27:871-880.
- Hilgetag CC, Theoret H, Pascual-Leone A (2001) Enhanced visual spatial attention ipsilateral to rTMS-induced 'virtual lesions' of human parietal cortex. *Nat Neurosci* 4:953-957.
- Hiscock M, Kinsbourne M (1977) Selective listening asymmetry in preschool children. *Dev Psychol* 13:217-224.
- Hiscock M, Lin J, Kinsbourne M (1996) Shifts in children's ear asymmetry during verbal and nonverbal auditory-visual association tasks: a 'virtual stimulus' effect. *Cortex* 32:367-374.
- Hiscock M, Cole LC, Benthall JG, Carlson VL, Ricketts JM (2000) Toward solving the inferential problem in laterality research: effects of increased reliability on the validity of the dichotic listening right-ear advantage. *J Int Neuropsychol Soc* 6:539-547.
- Hoff H, Pözl O (1937) Ueber eine optisch-agnostische Störung des 'Psiognomie-Gedächtnisses'. *Z Ges Neurol Psychiat* 159:367-395.
- Hough MS, Daniel HJ, Snow MA, O'Brien KF, Hume WG (1994) Gender differences in laterality patterns for speaking and singing. *Neuropsychologia* 32:1067-1078.
- Hugdahl K (2000) Lateralization of cognitive processes in the brain. *Acta Psychol* 105:211-235.
- Hughlin Jackson J (1874) On the nature of the duality of the brain. *Med Press Circ* 17, 19, 41, 63. [Reprinted in 1915 in *Brain* 38:80-103.]
- Hughlin Jackson J (1876) Case of large cerebral tumour without optic neuritis, and with left hemiplegia and imperception. *Roy Ophthalm Hosp Rep* 8:434-444. [Reprinted in 1932 in *Selected writings*, vol. 2, pp. 146-252. London: Taylor.]
- Inglis J, Lawson JS (1981) Sex differences in the effects of unilateral brain damage on intelligence. *Science* 212:693-695.
- Josse G, Tzourio-Mazoyer N (2004) Hemispheric specialization for language. *Brain Res Brain Res Rev* 44:1-12.
- Kinsbourne M, Bruce R (1987) Shift in visual laterality within blocks of trials. *Acta Psychol* 66:139-155.
- Kleist K (1923) Kriegsverletzungen des Gehirns in ihrer Bedeutung für die Hirnlokalisation und Hirnpathologie. In: *Handbuch der ärztlichen Erfahrung im Weltkriege 1914-1918*. Vol. 4. Geistes- und Nervenkrankheiten (Schjerning O, ed.). Leipzig: Barth.
- Koenig T, Prichep L, Lehmann D, Sosa PV, Braecker E, Kleinlogel H, Isenhardt R, John ER (2002) Millisecond by millisecond, year by year: normative EEG microstates and developmental stages. *Neuroimage* 16:41-48.
- Kondákor I, Pascual-Marqui RD, Michel CM, Lehmann D (1995) Event-related potential map differences depend on the prestimulus microstates. *J Med Eng Technol* 19:66-69.
- Kondákor I, Lehmann D, Michel CM, Brandeis D, Kochi K, Koenig T (1997) Prestimulus EEG microstates influence visual event-related potential microstates in field maps with 47 channels. *J Neural Transm* 104:161-173.
- Koukkou M, Lehmann D (1987) An information-processing perspective of psychophysiological measurements. *J Psychophysiol* 1:109-112.
- Kulynych JJ, Vadar K, Jones DW, Weinberger DR (1994) Gender differences in the normal lateralization of the supratemporal cortex: MRI surface-rendering morphometry of Heschl's gyrus and the planum temporale. *Cereb Cortex* 4:107-118.
- Landis T, Graves R, Goodglass H (1982) Aphasie reading and writing: possible evidence for right hemisphere participation. *Cortex* 18:105-112.
- Lehmann D (1987) Principles of spatial analysis. In: *Handbook of electroencephalography and clinical neurophysiology*. Vol. 1. Methods of analysis of brain electrical and magnetic signals (Gevin AS, Rémond A, eds), pp. 309-354. Amsterdam: Elsevier.
- Lehmann D, Skrandies W (1980) Reference-free identification of components of checkerboard-evoked multichannel potential fields. *Electroencephalogr Clin Neurophysiol* 48:609-621.
- Lehmann D, Michel CM, Pal I, Pascual-Marqui RD (1994) Event-related potential maps depend on prestimulus brain electric microstate map. *Int J Neurosci* 74:239-248.
- Liepmann H (1900) Das Krankheitsbild der Apraxie (motorische Aymbolie). *Monatsschr Psychiat Neurol* 8:15-44, 102-132.
- Marshall J, Caplan D, Holmes J (1975) The measure of laterality. *Neuropsychologia* 13:315-321.
- McCormick CM, Teillon SM (2001) Menstrual cycle variation in spatial ability: relation to salivary cortisol levels. *Horm Behav* 39:29-38.
- McGlone J (1977) Sex differences in the cerebral organization of verbal functions in patients with unilateral brain lesions. *Brain* 100:775-793.
- McGlone J (1980) Sex differences in human brain asymmetry: a critical survey. *Behav Brain Sci* 3:215-63.
- Meinschaefer J, Hausmann M, Güntürkün O (1999) Laterality effects in the processing of syllable structure. *Brain Lang* 70:287-293.
- Michel CM, Seeck M, Landis T (1999) Spatiotemporal Dynamics of Human Cognition. *News Physiol Sci* 14:206-214.
- Müller MM, Malinowski P, Gruber T, Hillyard SA (2003) Sustained division of the attentional spotlight. *Nature* 424:309-312.
- Oldfield RC (1971) The assessment and analysis of handedness: the Edinburgh Inventory. *Neuropsychologia* 9:97-113.
- Ortigue S, Michel CM, Murray MM, Mohr C, Carbonnel S, Landis T (2004) Early spatio-temporal dynamic of emotional words. *Neuroimage* 21:1242-1251.
- Pascual-Marqui RD, Michel CM, Lehmann D (1995) Segmentation of brain electrical activity into microstates: model estimation and validation. *IEEE Trans Biomed Eng* 42:658-665.
- Perrin F, Pernier J, Bertrand O, Giard MH, Echallier JF (1987) Mapping of scalp potentials by surface spline interpolation. *Electroencephalogr Clin Neurophysiol* 66:75-81.
- Pizzamiglio L, Mammucari A, Razzano C (1985) Evidence for sex differences in brain organization in recovery in aphasia. *Brain Lang* 25:213-223.
- Poffenberger A (1912) Reaction time to retinal stimulation with special reference to the time lost in conduction through nervous centers. *Arch Psychol* 23:1-73.
- Pommé A, Janny P (1954) Trouble de la mémoire topographique consécutif à une intervention sur l'hémisphère non dominant. *Rev Neurol* 91:307-308.
- Poppelreuter W (1917) Die psychischen Schädigungen durch Kopfschuss im Krieg 1914/16 Mit besonderer Berücksichtigung der pathopsychologischen, pädagogischen, gewerblichen und sozialen Beziehungen, Vol 1. In: *Die Störungen der niederen und höheren Schleistungen durch Verletzungen des Okzipitalhirns*. Leipzig: Voss.
- Purdon SE, Klein S, Flor-Henry P (2001) Menstrual effects on asymmetrical olfactory acuity. *J Int Neuropsychol Soc* 7:703-709.
- Regard M, Cook ND, Wieser HG, Landis T (1994) The dynamics of cerebral dominance during unilateral limbic seizures. *Brain* 117:91-104.
- Ross ED (1981) The aprosodias. Functional-anatomic organization of the affective components of language in the right hemisphere. *Arch Neurol* 38:561-569.
- Rossell SL, Bullmore ET, Williams SCR, David AS (2002) Sex differences in functional brain activation during a lexical visual field task. *Brain Lang* 80:97-105.
- Satz P (1977) Laterality tests: an inferential problem. *Cortex* 6:430-439.

- Shapleske J, Rossell SL, Woodruff PW, David AS (1999) The planum temporale: a systematic, quantitative review of its structural, functional and clinical significance. *Brain Res Brain Res Rev* 29:26-49.
- Shaywitz BA, Shaywitz SE, Pugh KR, Constable RT, Skudlarski P, Fulbright RK, Bronen RA, Fletcher JM, Shankweiler DP, Katz L, Gore JC (1995) Sex differences in the functional organization of the brain for language. *Nature* 373:607-609.
- Spellacy F, Blumstein S (1970) The influence of language set on ear preference in phoneme recognition. *Cortex* 6:430-439.
- Sperry RW, Gazzaniga MS, Bogen JE (1969) Interhemispheric relationships: the neocortical commissures; syndromes of hemispheric disconnection. In: *Handbook of clinical neurology* (Vinken PJ, Brujn GW, eds), vol. 4, pp. 273-290. Amsterdam: North Holland.
- Springer SP, Deutsch G (1981) *Left brain, right brain*. San Francisco, CA: WH Freeman.
- Strauss E (1983) Perception of emotional words. *Neuropsychologia* 21:99-103.
- Super H, van der Togt C, Spekreijse H, Lamme VA (2003) Internal state of monkey primary visual cortex (V1) predicts figure-ground perception. *J Neurosci* 23:3407-3414.
- Taylor KI, Regard M (2003) Language in the right cerebral hemisphere: contributions from reading studies. *News Physiol Sci* 18:257-261.
- Teng EL (1981) Dichotic ear difference is a poor index for the functional asymmetry between cerebral hemispheres. *Neuropsychologia* 19:235-240.
- Turkewitz G, Ross P (1983) Changes in visual field advantage for facial recognition: the development of a general processing strategy. *Cortex* 19:179-185.
- Wackermann J, Lehmann D, Michel CM, Strik WK (1993) Adaptive segmentation of spontaneous EEG map series into spatially defined microstates. *Int J Psychophysiol* 14:269-283.
- Wada JA, Clark R, Hamm A (1975) Cerebral hemisphere asymmetry in humans. *Arch Neurol* 32:239-246.
- Wernicke C (1874) *Der Aphasische Sprachenkomplex*. Breslau: Max Cohn & Weigert.
- Wigan AL (1844) *A new view of insanity: the duality of the mind*. London: Longman, Brown, Green & Longmans. [Reprinted by J Simon, Malibu, 1985.]
- Windmann S, Daum I, Güntürkün O (2002) Dissociating prelexical and postlexical processing of affective information in the two hemispheres: effects of the stimulus presentation format. *Brain Lang* 80:269-286.
- Zaidel E (1983) Disconnection syndrome as a model for laterality effects in the normal brain. In: *Cerebral hemisphere asymmetry*, pp. 95-151. (Hellige J, ed.). New York: Praeger Publishers.