

On females' lateral and males' bilateral activation during language production: A fMRI study

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Abstract

This study focuses on sex/gender and language in fMRI research. We explore the question of similarities and differences in 22 men and 22 women, respectively, in a fMRI language production task of fluent narration in which covert language production was contrasted with an auditory attentional task. In women, a left-lateralised activation concentrated in BA 44 while in men activation was more frontal in BA 45 and more often bilateral. This result is the opposite of those shown so far. Interestingly, the effect is only significant at the level of group analysis; it disappears when analysing activation at the level of the individual subject. We argue that sex/gender differences in the brain should be regarded much more critically, due to the numerous variables interacting and thus confounding with sex/gender. Our present study, too, cannot resolve the controversy about the existence of sex/gender similarities and differences in fMRI-language investigations.

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1. Introduction

The existence of sex/gender-differences during cognitive tasks as revealed by functional imaging is highly controversial. Gender studies indicate that there does not exist a clear-cut distinction between sex and gender (Butler, 1990). Also in the investigations described here, i.e. language representation, the biological and the sociological components for the observed activity cannot be easily differentiated. We, therefore, try to express this by using the double-term sex/gender wherever applicable.

With respect to language processing, numerous studies have been carried out in the course of the last 10 years with a variety of approaches, different techniques, and divergent results. A first investigation (Shaywitz et al., 1995) demonstrated sex/gender associated differences in lateralisation in one of several tested language tasks. With the exception of the large survey by Frost et al. (1999), which did not reveal sex/gender differences, demonstrating differences in lateralisation between women

and men dominated fMRI-based language research (Kansaku et al., 2000; Kansaku and Kitazawa, 2001; Phillips et al., 2001; Baxter et al., 2003; see Table 1 listing investigations explicitly addressing the sex/gender issue by means of fMRI). More recent studies using large sample sizes (as in Frost et al., 1999) do not exhibit any sex/gender-based dissimilarities (Weiss et al., 2003; Plante et al., 2005) nor did the meta-analysis by Sommer et al. (2004). The latter study includes a number of investigations, which did not set out from the sex/gender question, but produced sex/gender related results as a by-product (e.g. Schlösser et al., 1998; Pujol et al., 1999; Pihlajamaki et al., 2000).

Conclusions about sex/gender-relevant particulars have been drawn from very different experimental approaches based on both, clinical and non-clinical research. Experimental designs considering a specific language task as only one variable among non-linguistic others may fail to assess human language in its immanent sense. For instance, Gur et al. (2000), who reported sex/gender differences in relation to task difficulty, asked subjects to answer to verbal associations in a verbal reasoning task. Linguistically, verbal associations are meant to be a part of the human language ability, but cannot be regarded as an essential feature of language processing. In fact, verbal

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Table 1
Sex/gender in fMRI studies on language processing

Authors	Task	Presence of differences in lateralisation	Areas exhibiting lateralisation differences	Number of subjects
Shaywitz et al. (1995)	Language perception: <i>orthographic, phonological, semantic</i>	Differences in orthographic task	F: IFG, orbital gyrus, both bilateral M: IFG, orbital gyrus, both lateral	38 (19 F, 19 M)
Frost et al. (1999)	Language perception: <i>auditory lexical-semantic</i>	No differences		100 (50 F, 50 M)
Kansaku et al. (2000)	Language perception: <i>listening (global structure)</i>	Differences in processing a narrative	F: bilateral MGT M: left STG, MGT	47 (25 F, 22 M)
Phillips et al. (2001)	Language perception: <i>passive listening</i>	Differences	F: bilateral ant., post. temporal lobe M: lateral ant., post. temporal lobe	20 (10 F, 10 M)
Baxter et al. (2003)	Language perception: <i>semantic language processing</i>	Differences	F: bilateral STG, left IFG M: left IFG, left STG, cingulate regions	19 (10 F, 9 M)
Weiss et al. (2003)	Language production: <i>word generation</i>	No differences		20 (10 F, 10 M)
Plante et al. (2005)	Language perception/production: <i>listening, phonology, word identification, verb generation</i>	Differences in sex × age		205 (101 F, 104 M)
Sommer et al. (2004)	Meta-analysis	No differences		819 (442 F, 377 M)

Investigations addressing explicitly the sex/gender question by means of fMRI language studies in healthy subjects (clinical studies not included). Difference in lateralisation means differences between bilateral versus lateral activation. When bilateralisation was found, it was in women. Abbreviations: F-female, IFG-inferior frontal gyrus, M-male, MGT-medial gyrus temporalis, STG-superior temporal gyrus.

associations may rather be considered as a judgment task, belonging to the cognitive system of decision-making rather than to the language system.

There have been many neuroimaging studies addressing the language system at a psycholinguistic level, without a defined focus on sex/gender. Most of these studies investigate sentence comprehension, testing different aspects of syntactic or/and semantic processing (Indefrey et al., 2001; Friederici et al., 2003). Sex/gender differences were detected primarily in complex comprehension tasks (Table 1). Language production – both in general studies on language processing (Franceschini et al., 2003) as well as with respect to sex/gender differences – is mostly restricted to word generation (Schlösser et al., 1998; Weiss et al., 2003), where subjects are instructed to generate words beginning with a given letter. Production of spontaneous speech (sentences or narrations), which classifies as natural language behaviour, is rarely employed. Of course language processing at sentence level has been investigated with fMRI (e.g. Haller et al., 2005). The types of sentences used (for instance ‘child throws ball’), however, can hardly be compared to spontaneous and natural language production as it occurs in free narration.

Linguistic studies propose that women have advantages in language production and verbal fluency (Halpern, 1992), while men are superior in the comprehension of verbal analogy (Hyde and Linn, 1988). Therefore, the aspect of task dependency should be given serious consideration. Differences in language tasks may produce different results with respect to sex/gender (Frost et al., 1999; Phillips et al., 2001), and thus represent a confounding variable in the object of investigation, i.e. language and sex/gender.

Most fMRI studies showing sex/gender differences state that their subjects did not reveal any differences in performance at the behavioural and psycholinguistic level (Shaywitz et al., 1995; Pugh et al., 1996; Frost et al., 1999; Kansaku et al., 2000; Kansaku and Kitazawa, 2001; Baxter et al., 2003; Weiss et al.,

2003). Most of them exhibited sex/gender differences in regional brain activation during language comprehension (Shaywitz et al., 1995; Pugh et al., 1996; Kansaku et al., 2000; Kansaku and Kitazawa, 2001; Phillips et al., 2001; Baxter et al., 2003). Up to now, only one fMRI study has focused explicitly on language production and sex/gender: Weiss et al. (2003) demonstrated that not sex/gender-related hemispheric organisation but task performance and therefore strategies for lexical verbal fluency are the reason for the different cortical patterns concerning the degree of lateralisation. Recently, Plante et al. (2005) also addressed the question of sex/gender based on a powerful experimental population of $N=205$ and on a broad variety of examined language tasks concerning both, language production and language perception. In their investigations, however, Plante et al. (2005) concentrated on the interaction of sex/gender with age.

In this paper, we examine the sex/gender question at the level of language production. Similar to Kansaku et al. (2000), we focus on the global structure of language, i.e. free narration as opposed to single words or isolated sentences. In line with several studies mentioned above (Shaywitz et al., 1995; Pugh et al., 1996; Schlösser et al., 1998; Baxter et al., 2003; Weiss et al., 2003), we explore the sex/gender differences and their relation to bi-/lateralisation in Broca’s area and its homologue in the right hemisphere, induced by the production of narratives. In fact, most of the studies cited concentrate on one aspect of sex/gender differentiation: the bi-/lateralisation in language areas of the brain. Many of them refer, in particular, to the bi-/lateralisation in Broca’s area (Shaywitz et al., 1995; Pugh et al., 1996; Schlösser et al., 1998; Baxter et al., 2003; Weiss et al., 2003). Although recent studies (Weiss et al., 2003; Sommer et al., 2004; Plante et al., 2005) did not find any difference, the notion of dissimilarities between the sexes/genders still dominates neuroscientific concepts. Therefore, it seems warranted to investigate the variable sex/gender at the level of

global language production in Broca's area and the Broca homologue in the right hemisphere.

2. Methods

2.1. Subjects

In the present fMRI study we examined 44 healthy, multilingual subjects with similar educational backgrounds (minimal requirement: undergraduate level), aged between 20 and 36 years. All of them were right-handed (Edinburgh Handedness Test). They gave written informed consent according to experimental/institutional guidelines and were paid a small remuneration. None of the subjects had any history of neurological disorders. The distribution of male and female participants in each group was balanced at 22. Language distribution in the first (native) language is given in Table 2.

2.2. Experimental task

The experimental task consisted in a silent free narration task and a baseline condition in a periodic block design adapted from Kim et al. (1997) and modified by Wattendorf et al. (2001). Stimuli for each task were presented visually: a cross for the baseline condition, images for the language condition. During the language condition which had been practiced in a previous training, subjects covertly told an imagined interlocutor what they had done the day before. The narration was supported by images of a rising sun, noon and a setting sun to help participants in telling fluently about the events during these three times of the previous day.

During the baseline condition, the volunteers performed an auditory attentional task triggered by the silent periods of the scanning sound occurring every 6 s, in which they were required to respond by a single finger tap. The main purpose of this control condition was to maintain attention rather than to

execute the motor act. It has been shown that such conditions do not involve much language network (Binder et al., 1999) and thus provide the optimal baseline, when a view on the entire language system is required. Each condition lasted 30 s and was repeated 9 times across a 9 min scanning schedule for each of the three languages the multilingual subjects were proficient in.

2.3. MRI data acquisition

Imaging was performed on a 1.5 T Magnetom Vision MRI scanner (Siemens, Germany). Functional images were obtained by using a T2*-weighted multislice echo planar imaging (EPI) sequence (repeat time: 6 s, echo time: 60 ms, flip angle: 90°) covering the entire brain with 48 contiguous axial slices (resolution: 3 × 3 × 3 mm), parallel to the AC–PC plane. In each language, 90 scans were collected comprising 9 blocks per condition. Each block included 5 scans. T1-weighted (resolution: 1 × 1 × 1 mm) anatomical images were acquired at the end of the functional imaging session using a MP-RAGE (magnetisation prepared rapid acquisition gradient echo) sequence.

2.4. Image analysis

For fMRI-analysis BrainVoyager 2000 (<http://www.brainvoyager.com>) was used. After pre-processing the raw data (3D motion correction, scaling of slice time by interpolation, 3D spatial data smoothing with Gaussian filter of 4.00 mm, temporal data smoothing with 3 cycles/points), second level statistical analysis was calculated for the 2 groups and for the 44 individual subjects.

The group analysis reported here used random effects (statistical threshold of p (uncorr) < 0.001) with separate study predictors for the main effect in the female and male group separately. Further, a fixed effect (statistical threshold of p (corr) < 0.05) for the interaction analysis (females vs. males) was carried out for a group comparison where female and male signal changes were combined into one general linear model. As described by Baxter et al. (2003), between group differences were determined by examining the main effect (females, males) and the interaction (females > males, males > females) designed to detect directional group differences. Sex effects were calculated based on a ROI-analysis in BA 44 and BA 45 derived from the random effect mentioned above. For females an individual female head template and for males an individual male template was used for both the main effect and the interaction effect.

A second analysis was based on the activation present in each individual subject in order to estimate the frequencies and degrees of women's and men's bilateral and left-lateralised activation. For this, all voxels activated at p (corr) < 0.05 in Broca's area and the right-sided Broca homologue were computed. Further, in bilateral subjects a lateralisation index (LI) was calculated to examine the degree of cortical lateralisation and to show potential misbalances in the bilateralised population, using the formula $LI = (L - R) / (L + R)$ where L is the amount of activated voxels within Broca's area and R is the amount of activated voxels within the Broca homologue in the right hemisphere (van der Kallen et al., 1998; Phillips et al., 2001).

Table 2
Language distribution in the first (native) language

	Women	Men
Swiss German	7	5
German	3	3
Italian	3	2
French	1	5
Spanish	1	3
English		2
Portuguese	1	
Catalan	1	
Turkish	1	
Hungarian	1	
Slovenian	1	
Bulgarian	1	
Finnish	1	
Greek		1
Serbo-Croatian		1

Our sample of multilingual subjects showed a large diversity of different native languages. Nevertheless, most of participants acquired one of the world languages Spanish, Italian, German (Swiss German), English or French as first language.

3. Results

3.1. General pattern of regional activation during the language condition

Our language production paradigm resulted in activation in numerous brain areas (see Fig. 1), in particular the perisylvian areas, including Broca's area and Wernicke's area (not shown). In addition, primary and secondary visual areas were activated as well as premotor and prefrontal areas, the supplementary motor area (SMA) and cingulate gyrus. In these cortical areas activation was always more pronounced on the left side. Subcortical activation was found in the basal ganglia. Activation in the cerebellum (not shown) was always contralateral to the activation in the frontal lobe. No effect of

the type of language on the regional activation in this language production task was noted (C. Bloch, E. Kuenzli, C. Nitsch, unpublished observations). In fact, with the exception of studies on reading and writing strategies in alphabetised versus non-alphabetised languages (Tan et al., 2003), differences between languages with a large linguistic distance were never noted in language production or comprehension tasks (e.g. Chee et al., 1999; Mahendra et al., 2003; Kim et al., 1997; Pu et al., 2001).

3.2. Group effect: main effect

Differences between the main effects of the two groups were noted for Broca's area in its lateralisation (Fig. 1A and B): women exhibit left lateralised activation ($x=-52, y=20, z=2$); p (uncorr) <0.001 and men bilateral activation ($x=52/-52,$

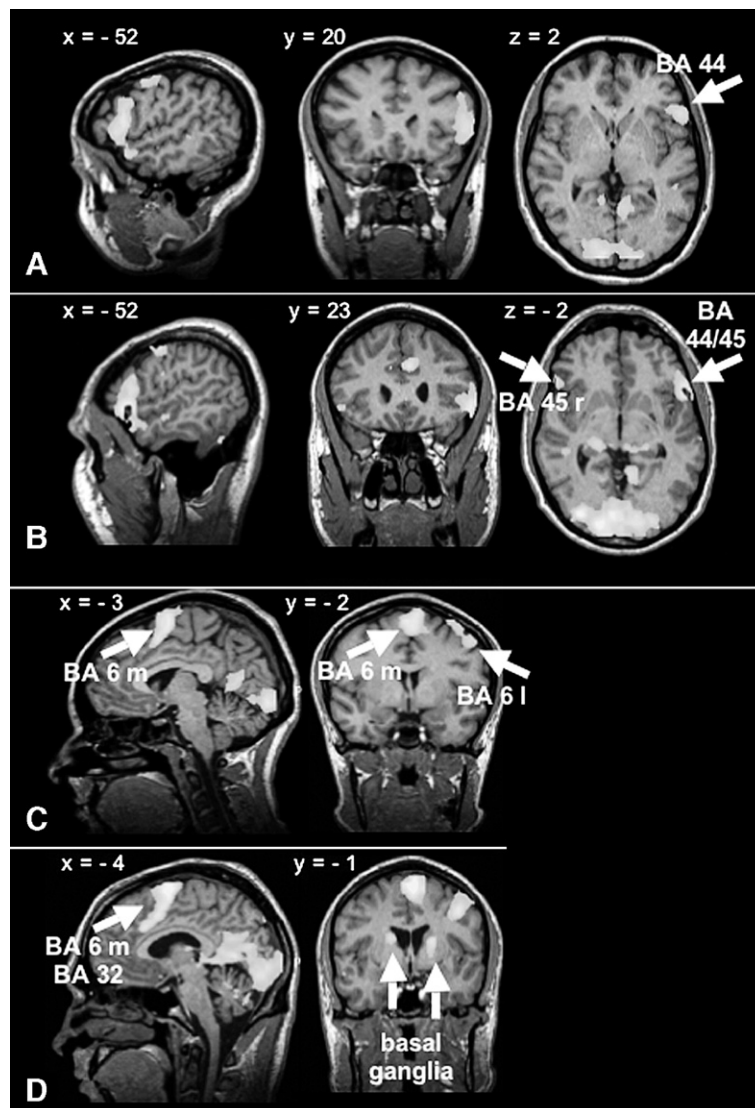


Fig. 1. Group analysis: main effect. Brain activation during language production was calculated at p (uncorr) <0.001 and is here indicated by various shades of light grey in the dark grey image of the brain. Coordinates for the main ROI are given on top of the single images. (A) In females, activation in Broca's area corresponds to BA 44. (B) In males, activation in left Broca's area is more frontal and basal, corresponding to BA 45. It is accompanied by activation in the contralateral Broca analogue (BA 45 r), as seen in the coronal and horizontal plane. (C) In females, activation in medial, supplementary motor area (BA6 m), as given by the coordinates, extends towards BA32 in the cingulate gyrus. It is accompanied by activation in the lateral premotor area (BA6 l). (D) In men, involvement of BA32 in the language processing is even more evident. In addition, a bilateral activation is present in the basal ganglia. Coordinates are given for the maximal activation in medial BA6.

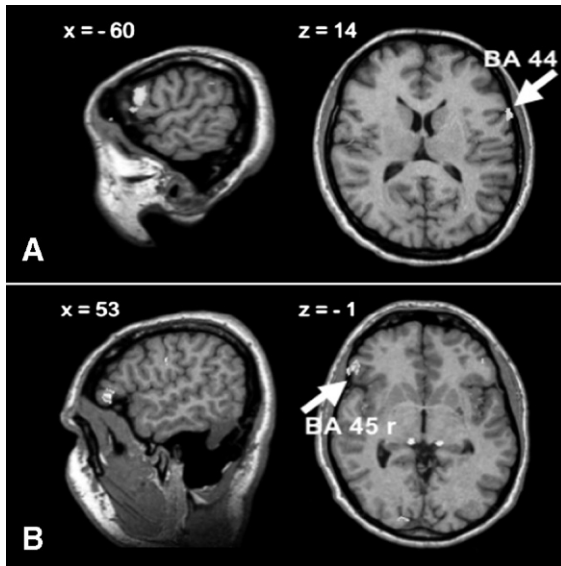


Fig. 2. Group analysis: interaction effect. The interaction effect was based on a fixed effect and calculated at p (corr) <0.05 . Coordinates for significant interaction (women $>$ men and men $>$ women) are given on top of the single images. (A) Women activate more left-sided Broca's area, BA 44, in particular. (B) Men activate more right-sided Broca's analogue, BA 45, in particular.

$y=23$, $z=-2$); p (uncorr) <0.001). Note that the activation in men is rather in the anterior part of Broca, i.e. in BA 45, and in women in the posterior part, BA 44. The uni-/bilateral activations in Broca's area were complemented by left-lateralised or bilateral activation in the basal ganglia (Fig. 1C and D) as well as by activation in medial BA 6, i.e. the supplementary motor area (Fig. 1C and D).

3.3. Group effect: interaction analysis

The observations concerning Broca's area were confirmed by the interaction analysis (Price et al., 1997). In women (females $>$ males) only the left-sided Broca's area showed activation at $x=-60$, $y=11$, $z=14$ (Fig. 2A). In men (males $>$ females) major activation in the right-sided Broca's homologue is present at $x=53$, $y=29$, $z=-1$ (Fig. 2B).

3.4. Individual analysis

To further examine the question of bi-/lateralisation we determined in each individual subject the number of activated

Table 3
Frequency distribution of lateralisation in Broca's area

	Women	Men
No activation	1	0
Left-lateralised–low	2	2
Left-lateralised–high	9	7
Bilateral–low	3	3
Bilateral–high	7	9
Right-lateralised–high	0	1

High describes a high significance level at p (corrected) <0.05 and *low* a lower significance level at p (uncorrected) <0.001 at which in each individual brain activation was found in Broca's area.

Table 4
Lateralisation index for bilaterally activating subjects

	Lateralisation index, Women (mean \pm SD)	Lateralisation index, Men (mean \pm SD)	p -value
BA 44	0.80 \pm 0.40	0.84 \pm 0.39	n.s.
BA 45	0.31 \pm 0.74	0.44 \pm 0.31	n.s.
Broca	0.52 \pm 0.59	0.53 \pm 0.27	n.s.

The lateralisation index (LI) was determined for BA 44, BA 45 and for Broca's area at p (corrected) <0.05 in every female and male independently and the mean values calculated. 1 means a maximal left-lateralisation (=0 activation on the right side), -1 a maximal right-lateralisation (=0 activation on the left side). $N=16$ for bilaterally activating subjects.

voxels in Broca's area. The individual variation was high and no significant differences were found between women and men in the activated subfields of Broca's area as well as in the degree of lateralisation as examined by Kruskal-Wallis and Mann-Whitney U -tests. We, therefore, solely based on the presence or absence of activation in the individual brain at the different significance levels of p (corr) <0.05 and p (uncorr) <0.001 , determined the frequency of bilateralisation and lateralisation in our total sample of subjects (Table 3). Seven females and nine males demonstrate bilateral patterns at a p (uncorr) <0.05 , while nine females and seven males showed left-lateralised activation. Thus, in contrast to the group comparisons, at the level of the single person the differences between men and women in bi-/lateralisation could not be replicated.

The degree of bilateralisation in Broca's area was determined for bilaterally activating individuals by calculating the lateralisation index (van der Kallen et al., 1998; Phillips et al., 2001). The degree of left lateralisation was larger in BA 44 than in BA 45 (Table 4). However, there was no sex/gender difference in bilaterally activating individuals. In women and men, the lateralisation index is positive, i.e. left lateralised.

4. Discussion

The first major result of this study is that, in contrast to all previous fMRI-based language studies, we observed in Broca's area, on average, bilateralisation in men but not in women. Moreover, in men activation was not only more frequently bilateral, but also more frontal, in BA 45, while in women the left-lateralised activation concentrated in BA 44. The second major result refers to the influence of the type of data analysis applied: Depending on the type of data analysis, i.e. group analysis versus individual analysis, sex/gender related similarities or differences may be obtained. In our study, group analysis enhanced the dissimilarities between the two groups, whereas the individual frequency analysis revealed similarities. While this may not be an exclusively fMRI-related aspect, it does have a special impact in fMRI research. Investigations in the field of cognition (in particular beyond clinical research) rarely perform analyses at an individual level, even less so fMRI-based language studies, which as yet have not considered the influence of individual variations when focusing on the sex/gender question.

As shown in the first part of our results, i.e. main effect and interaction analysis, group-based analyses tend to reinforce

group-based bi-/lateralisation. Firstly, these analyses resulted in a bilateralised activation in men versus a left-lateral activation in women in Broca's area. Secondly, they showed an increased left activation in BA 44 in women in contrast to the stronger activation in the right BA 45 homologue in men. Thirdly, a powerful left lateralisation was revealed in women, and a less pronounced left/right difference in men. By shifting the focus in the analysis from the group to the individual, as seen in the frequency analysis and in the lateralisation index, differences in lateralisation become much less detectable. The female to male distribution of 9:7 versus 7:9 in lateralisation and bilateralisation, respectively, is much less pronounced than implied by the group analysis. Only a minority of the subjects ($N=16$) exhibits bilateral activation at all. Furthermore, these are found in both sexes/genders, in women and in men. This result is confirmed by the lateralisation index, which considers primarily the individual and does not show a difference between bilaterally activating females and males: both exhibiting a positive index, i.e. a left-sided misbalance.

Lateralised female and bilateral male activation can be explained in several ways, all of them outlining different variables of influence, such as task specificity, methods used to measure asymmetry, performance level, as well as language and problem-solving strategies. Here, we show that the factor group versus single subject analysis may play a significant role, too. In the following discussion we will address some critical points in designing and interpreting studies on sex/gender differences in language-related fMRI-research.

Task specificity as a key variable in eliciting sex/gender relevant results has been highlighted repeatedly (Frost et al., 1999; Kansaku and Kitazawa, 2001; Phillips et al., 2001). Phillips et al. (2001), although demonstrating sex/gender differences with respect to bi-/lateralisation of activations in the anterior and posterior temporal lobe during an auditory comprehension task, critically discuss task specificity, as well as possible experimentally based sex/gender biases concerning fMRI methods. They criticise the methods used to measure asymmetries, such as ROI analysis of significance threshold maps, and show how this specific approach increases systematically the asymmetries as the threshold increases. Consequently, they propose a threshold independent method for determining the activation: the measurement of peak percentage activation.

One central aspect of neuroimaging studies on sex/gender is to find out whether the sex/gender variable is independent of performance levels (Weiss et al., 2003). Independence of performance level would suggest that women and men carry out identical language processes with the same degree of functional capacity supported however by very differently organised brain systems. As mentioned above, hardly any fMRI language studies on sex/gender showed differences at the behavioural and psycholinguistic level (Shaywitz et al., 1995; Pugh et al., 1996; Frost et al., 1999; Kansaku et al., 2000; Kansaku and Kitazawa, 2001; Baxter et al., 2003; Weiss et al., 2003). Weiss et al. (2003) argued that sex/gender specific differences in the cerebral organisation of language functions are absent when subjects are matched for performance in language tasks. While our subjects were not administered any specific language test on the

performance level in their first language (L1), language samples were recorded after the fMRI experiment. Rather than on performance in the sense of linguistic correctness, free narration depends on fluency. We therefore calculated fluency in terms of produced number of syllables per time unit. No significant differences were revealed in our sample (D. Zappatore, unpublished data). It therefore seems unlikely that differences in performance are causing the differences in lateralisation and in engagement of the subfields of Broca's area. Rather, this may indicate that different strategies are employed.

Other studies, not solely on language but using mental rotation tasks (Jordan et al., 2002) or memory tasks (Gaab et al., 2003), have demonstrated the importance of strategies as a variable influencing the sex/gender-dependent brain activation. They all argue that not sex/gender, but the applied sex/gender-dependent strategy determines differences in brain activation. The factors causing sex/gender-dependent strategies are not established, although the role of sex/gender-dependent socialisation could be a crucial factor (see Schmitz, 1999).

Recently age has been suggested as an additional variable: Plante et al. (2005) do not show significant differences in the degree of lateralisation in the classical left hemisphere language areas of the brain and their right homologues, but emphasise as the first fMRI study in language processing, the importance of age as a determining factor in cortical language representation in connection with the sex/gender and the bi-/lateralisation debate.

Independently of the above-cited variables, only one study on this topic denies the existence of sex/gender differences on a macroscopic level and therefore detectable by fMRI at all (Frost et al., 1999). By contrasting the female/male groups with two groups of randomly assigned subjects, Frost et al. (1999) examined the overall activation patterns as well as regions of interest in lateralised and in intrahemispheric cortical activation patterns. As no differences were found, the authors argue against substantial differences in the neuroanatomical organisation of language processing in women and men.

Finally, the meta-analysis of Sommer et al. (2004) should be considered. They investigated whether language representation is indeed more bilateral in the female than in the male brain in a sample of 14 studies, providing data on 442 women and 377 men without finding any significant difference in language lateralisation between females and males. However, data from clinical studies were also included, what can be seen as a problematic factor. Clinical studies enlarge the probability of finding differences. They are meant to examine primarily patients with a history of language disability, but including sex/gender increases the possible combinations of comparison. Thus, the number of compared groups can be quadruplicated from experimental group versus control group to female experimental group versus female control group, male experimental group versus male control group, female experimental versus male experimental group, and female control group versus male experimental group (see also van der Kallen et al., 1998). In each of these compared pairs, there are differences to be detected, and this is an explicit aim in experimental studies.

Linked to last point, additional factors may need to be taken into account, such as scientific-pragmatic ones, which influence

the “fate” of studies in neuroimaging and in sex/gender research. Thus, numerous studies proving the null hypothesis, i.e. showing an “absence of sex effects in language processing may never have been published.” (Binder et al., 2000, p. 405). Binder et al. (2000) criticise this kind of publication bias (see also Dickersin and Min, 1993). Such a publication bias might indeed mask evidence on sex/gender similarities.

Taken together, the question about sex/gender similarities and differences in the brain during language processing is dependent on a great number of variables, which can lead both to evidence for bilateralisation as well as for lateralisation in women or in men. It is therefore of high importance in this field of research to critically reflect on the design and on the analyses to be employed when devising an experiment to investigate the sex/gender-question.

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References

- Baxter, L., Saykin, A., Flashman, L., Johnson, S., Guerin, S., Babcock, D., Wishart, H., 2003. Sex differences in semantic language processing: a functional MRI study. *Brain Lang.* 84, 264–272.
- Binder, J., Frost, J., Hammeke, T., Bellgowan, P., Rao, S., Cox, R., 1999. Conceptual processing during the conscious resting state: a functional MRI study. *J. Cogn. Neurosci.* 11, 80–93.
- Binder, J., Frost, J., Hammeke, T., Springer, J., Bellgowan, P., Rao, S., Cox, R., 2000. Language processing in both sexes: evidence from brain studies (Reply to J. Harasty). *Brain* 123, 405–406.
- Butler, J., 1990. *Gender Trouble: Feminism and the Subversion of Identity*. Routledge, London.
- Chee, M., Tan, E., Thiel, T., 1999. Mandarin and English single word processing studied with functional magnetic resonance imaging. *J. Neurosci.* 19, 3050–3056.
- Dickersin, K., Min, Y., 1993. Publication bias: the problem that won't go away. *Ann. N. Y. Acad. Sci.* 703, 135–146 discussion 146–148.
- Franceschini, R., Zappatore, D., Nitsch, C., 2003. Lexicon in the brain: what neurobiology has to say about languages. In: Cenoz, J., Hufeisen, B., Jessner, U. (Eds.), *The Multilingual Lexicon*, Dordrecht, pp. 153–166.
- Friederici, A., Ruschemeyer, S., Hahne, A., Fiebach, C., 2003. The role of left inferior frontal and superior temporal cortex in sentence comprehension: localizing syntactic and semantic processes. *Cereb. Cortex* 13, 170–177.
- Frost, J., Binder, J., Springer, J., Hammeke, T., Bellgowan, P., Rao, S., Cox, R., 1999. Language processing is strongly left lateralized in both sexes. Evidence from functional MRI. *Brain* 122, 199–208.
- Gaab, N., Keenan, J., Schlaug, G., 2003. The effects of gender on the neural substrates of pitch memory. *J. Cogn. Neurosci.* 15, 810–820.
- Gur, R., Alsop, D., Glahn, D., Petty, R., Swanson, C., Maldjian, J., Turetsky, B., Detre, J., Gee, J., Gur, R., 2000. An fMRI study of sex differences in regional activation to a verbal and a spatial task. *Brain Lang.* 74, 157–170.
- Haller, S., Radue, E.W., Erb, M., Grodd, W., Kircher, T., 2005. Overt sentence production in event-related fMRI. *Neuropsychologia* 43, 807–814.
- Halpern, D., 1992. *Sex Differences in Cognitive Abilities*, 2nd ed. Lawrence Erlbaum, Hillsdale (NJ).
- Hyde, J., Linn, M., 1988. Gender differences in verbal ability: a meta-analysis. *Psychol. Bull.* 104, 53–69.
- Indefrey, P., Hagoort, P., Herzog, H., Seitz, R., Brown, C., 2001. Syntactic processing in left prefrontal cortex is independent of lexical meaning. *NeuroImage* 14, 546–555.
- Jordan, K., Wüstenberg, T., Heinze, H., Peters, M., Jäncke, L., 2002. Women and men exhibit different cortical activation patterns during mental rotation tasks. *Neuropsychologia* 40, 2397–2408.
- Kansaku, K., Kitazawa, S., 2001. Imaging studies on sex differences in the lateralization of language. *Neurosci. Res.* 41, 333–337.
- Kansaku, K., Yamaura, A., Kitazawa, S., 2000. Sex differences in lateralization revealed in the posterior language areas. *Cereb. Cortex* 10, 866–872.
- Kim, K., Relkin, N., Lee, K., Hirsch, J., 1997. Distinct cortical areas associated with native and second languages. *Nature* 388, 171–174.
- Mahendra, N., Plante, E., Magloire, J., Milman, L., Trouard, T., 2003. fMRI variability and the localization of languages in the bilingual brain. *NeuroReport* 14 (9), 1225–1228.
- Phillips, M., Lowe, M., Lurito, J., Dzemidzic, M., Mathews, V., 2001. Temporal lobe activation demonstrates sex-based differences during passive listening. *Radiology* 220, 202–207.
- Pihlajamäki, M., Tanila, H., Hanninen, T., Kononen, M., Laakso, M., Partanen, K., Soininen, H., Aronen, H.J., 2000. Verbal fluency activates the left medial temporal lobe: a functional magnetic resonance imaging study. *Ann. Neurol.* 47, 470–476.
- Plante, E., Schmithorst, V., Holland, S., Byars, A., 2005. Sex differences in the activation of language cortex during childhood. *Neuropsychologia* 44 (7), 1210–1221.
- Price, C., Moore, C., Friston, K., 1997. Subtractions, conjunctions, and interactions in experimental design of activation studies. *Human Brain Mapping* 5, 264–272.
- Pu, Y., Liu, H., Spinks, J., Mahankali, S., Xiong, J., Feng, C., Tan, L., Fox, P., Gao, J., 2001. Cerebral hemodynamic response in Chinese (first) and English (second) language processing revealed by event-related functional MRI. *Magn. Reson. Imaging* 19 (5), 643–647.
- Pugh, K., Shaywitz, B., Shaywitz, S., Constable, R., Skudlarski, P., Fulbright, R., Bronen, R., Shankweiler, D., Katz, L., Fletcher, J., Gore, J., 1996. Cerebral organization of component processes in reading. *Brain* 119, 1221–1238.
- Pujol, J., Deus, J., Losilla, J.M., Capdevila, A., 1999. Cerebral lateralization of language in normal left-handed people studied by functional MRI. *Neurology* 52, 1038–1043.
- Schlösser, R., Hutchinson, M., Joseffer, S., Rusinek, H., Saarimäki, A., Stevenson, J., Dewey, S., Brodie, J., 1998. Functional magnetic resonance imaging of human brain activity in a verbal fluency task. *J. Neurol. Neurosurg. Psychiatry* 64, 492–498.
- Schmitz, S., 1999. Gender differences in the acquisition of environmental knowledge related to wayfinding behavior, spatial anxiety and self-estimated environmental competencies. *Sex Roles* 41, 71–93.
- Shaywitz, B., Shaywitz, S., Pugh, K., Constable, R., Skudlarski, P., Fulbright, R., Bronen, R., Fletcher, J., Shankweiler, D., Katz, L., et al., 1995. Sex differences in the functional organization of the brain for language. *Nature* 373, 607–609.
- Sommer, I., Aleman, A., Bouma, A., Kahn, R., 2004. Do women really have more bilateral language representation than men? A meta-analysis of functional imaging studies. *Brain* 127, 1845–1852.
- Tan, L., Spinks, J., Feng, C., Siok, W., Perfetti, C., Xiong, J., Fox, P., Gao, J., 2003. Neural systems of second language reading are shaped by native language. *Hum. Brain Mapp.* 18 (3), 158–166.
- van der Kallen, B., Morris, G., Yetkin, F., van Erming, L., Thijssen, H., Haughton, V., 1998. Hemispheric language dominance studied with functional MR: preliminary study in healthy volunteers and patients with epilepsy. *Am. J. Neuroradiol.* 19, 73–77.
- Wattendorf, E., Westermann, B., Zappatore, D., Franceschini, R., Lüdi, G., Radue, E.W., Nitsch, C., 2001. Different languages activate different subfields in Broca's area. *NeuroImage* 13 (6), 624.
- Weiss, E., Siedentopf, C., Hofer, A., Deisenhammer, E., Hoptman, M., Kremser, C., Golaszewski, S., Felber, S., Fleischhacker, W., Delazer, M., 2003. Brain activation pattern during a verbal fluency test in healthy male and female volunteers: a functional magnetic resonance imaging study. *Neurosci. Lett.* 352, 191–194.